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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

PUBLIC HEALTH. 1961, Mar., v. 75, No. 3, 129–84, 4 figs. [20 refs.] **Environmental Health Today.**

Since October 1960 *Public Health* the Journal of the Society of Medical Officers of Health has appeared at two-monthly, instead of monthly, intervals; each issue contains more pages and tends to devote the whole of a number to a single subject. The March 1961 issue deals with "Environmental Health Today" and contains 6 outstanding papers. The editorial puts the matter into perspective and expresses concern about those who "decry the importance of taking problems of physical environment seriously." The papers make it clear that the old problems exist though the shape of the problems may have changed.

The first paper *The Public Health* by Sir John CHARLES (pp. 131–38) is a scholarly account of references to public health in classical writings including those of Aristotle, Hippocrates, Celsus and the architect Vitruvius (B.C 76–B.C. 11). It then proceeds to England in the 19th century and the ideas of Jeremy Bentham and Edwin Chadwick supported by the 3 doctors, Neil Arnott, James Philip Kay-Shuttleworth and Thomas Southwood Smith. Their reports resulted in the first Public Health Act, that of 1848. Then, after the departure from office in 1854 of Chadwick, came the great protagonist of public health John Simon.

The second paper (pp. 139–49), on *Administration and Organization of the Environmental Health Services* is by Edward HUGHES, Medical Officer of Health of Reading. In a chart he sets out the administrative structure of the Ministry of Housing and Local Government and its relationship to other ministries: another chart does the same for the Ministry of Agriculture, Fisheries and Food and 2 others give in diagrammatic form the legal side of housing work and the prevention of atmospheric pollution. The author stresses the need for assistant medical officers of health to be trained in environmental health work and suggests how this can be done.

In a section on specialization it is noted that, except in the very largest authorities, there is very little among the medical public health staff but that it is commoner among the public health inspectorate and is justified for housing, atmospheric pollution, meat inspection, food and drugs sampling and port health work. In Reading, the specialist inspectors are given the rank of senior and are periodically given a spell of general duties in a district. A plea is made for leg work as opposed to motor car transport for those engaged in district work. On the controversial point of the relationship between the MOH and the public health inspector—a recurring theme in this series of papers—it should be the function of the MOH to plan the strategy and the chief public health inspector the tactics. In most areas there is good team work and no friction but the position becomes difficult when the MOH is a "social medicine addict" who is quite happy to leave sanitary matters to the inspectors and then complains if symptoms of separationism arise. But, the MOH must do a share of the field work and take a real interest in environmental hygiene.

The third article (pp. 149–58) is on *Housing—Past Present and Future* by J. SARGINSON and C. H. SHAW. It is a valuable review of housing legislation and procedure based mainly on Sheffield experience; a city which grew rapidly 80 to 100 years ago and where the houses then built are becoming worn out. Some more recently built are becoming obsolescent and as the owners, except for some owner-occupiers, make little use of the improvement grant procedure it is suggested that local authorities should, by agreement, purchase blocks of decaying but originally well built property and themselves carry out any needed improvements which may include making self-contained flats out of big houses too large for present needs. The intricacies of clearance and redevelopment procedures are well described. In the country as a whole 40% of unfit houses are dealt with by individual demolition orders; in Sheffield preference is given to including them in larger development schemes and their percentage of orders for individual houses is only 3. The difficulties which arise from the retention in current legislation of the term "dangerous or injurious to the health of the inhabitants" lead to the question whether the MOH is necessarily the right person to initiate a clearance

scheme. In Sheffield the senior officers concerned, headed by the Town Clerk, meet weekly to consider all matters concerning slum clearance and redevelopment. More attention is now being paid to the housing of the aged and the national percentage of single bedroomed houses completed by local authorities has risen from 7 in 1945–56 to 28 in the first half of 1960. A shared bathroom and WC is considered suitable for this type of tenant. Welfare authorities have power under the National Assistance Act, 1948, to adapt houses so that they meet the needs of disabled persons and much is being done in Sheffield. It is useful to house the aged and the disabled on the same site as both need central heating and the services of a warden. But there should be normal housing as part of the estate and the ratio of the disabled to the aged about 1 to 6. In all new housing it is worth paying the extra cost for sound-proofing. Present housing policy does not allow for a 3 generation family to live together. The suggestion is made that they might be brought together again by providing two fully independent units adjoining each other but with a communicating door normally kept locked.

The fourth (pp. 159–68) is *Some County District Problems in a Favoured Area* by D. J. N. McNab. The "favoured area" adjoins Bournemouth and its population increased during the last 15 years by 23% to 49% in different districts. The problems discussed are water supply which is becoming overtaxed: sewage disposal which means new sewers and a decision whether the former method of disposal by running the sewage into the sea, with the aesthetic, if not health, damage to the sea front should be continued: refuse disposal with the problem of finding suitable land for controlled tipping: housing, as at one time there were 546 families living in Nissen-hutted camps redundant after the war; many have been rehoused but there is a residue of problem families living in sub-standard accommodation. A separate problem is that the district is popular with day trippers. There are many eating houses to cater for them and it is difficult to maintain even elementary standards of food hygiene in the height of the season. The trippers leave litter behind them which has to be collected and disposed of. There is a long section on caravans: some are truly mobile but others are used as permanent homes. There are in the area 3,000 caravans on 48 licensed sites; 800 are permanent homes; fortunately the families contain few children.

Beach huts require supervision and a special problem in this area is caused by the presence of the "New Forest Gipsies" among whose children infestation with round worms is prevalent. Housing presents special problems in rural areas: in this one, in the last 6 years 141 unfit houses have been closed and 152 made fit for human habitation.

The fifth (pp. 168–75) is by W. R. Martine on *Food Hygiene and the Medical Officer of Health.* It maintains that efficient public health practice is a blend of the personal and the environmental health services and regrets that those whose main interest was hospital administration did not, after 1948, develop a reawakened interest in environmental hygiene. There is much work for the MOH in the administration of the Food Hygiene Regulations of 1955 and he should not leave it all to the public health inspector. The author points out that there is no national requirement for the registration of an eating house and no ban on dogs and cats in food shops. He is concerned about watercress and cream. It is essential that both the general public and all engaged in the various food trades should receive education in hygienic practices.

The 6th and last paper (pp. 176–84) is by J. H. C. Clarke, MOH of parts of Kesteven, Lincolnshire, on *The Control of Public Water Supplies from the Public Health Standpoint.* It is mainly concerned with regional water schemes in rural areas. The author made a detailed survey of water supplies throughout his county in 1945. Since then the daily consumption of water per head has risen from 6 to 10 gallons per head to 30–40. There is no shortage of water but there is of money and materials to take water to houses and farms. Nevertheless 95% of the population of England and Wales have a piped supply of water which is higher than in any other country.

There is an interesting note on infant methaemoglobinaemia due to water. In Suffolk in 1950 there were 3 cases and one death. The author recalls from his own experience contamination of a water supply by sewage effluent; and contamination of the water supply of a Midland city by a threadworm, "Nais." The final section deals with the practical aspects of the artificial fluoridation of a public water supply.

Allen Daley

Warren, M. D. **Social and Preventive Medicine.** *Brit. J. Clin. Practice.* 1961, Mar., v. 15, No. 3, 217–27.

This is an account of the teaching of social and preventive medicine at the Medical School of the Royal Free Hospital, London. The author holds a joint appointment at the Royal Free (70% of his time) and the London School of Hygiene and Tropical Medicine (30%).

The recommendations of the Goodenough Committee on Medical Education and the requirements of the General Medical Council are set out.

The aims and objects of the Royal Free teaching are (1) "To demonstrate aspects of the aggregate of illness within the community"; (2) "To broaden the student's approach to a patient" and "gain insight into the social and psychological implications of an episode of illness"; (3) "To introduce the student to the broad outlines of the health, medical, social and welfare services"; (4) "To demonstrate the genetic, social and environmental factors operating in the causation of illness"; (5) "To make a study of healthy people and communities."

At the Royal Free the students, after passing their pre-clinical examination, attend for 10 weeks an introductory course on case taking: during this period they have 8 lectures on social and preventive medicine, one being given by the chief almoner. The students visit the offices of the almoners and acquaint themselves with the type of work they do: they, also, pay a visit to the local public health department. In the "Junior Medicine" course which follows one patient is selected by

the medical registrar and the almoner for detailed study. This involves a visit to the patient's home and discussion with the general practitioner. It may involve a visit to the disablement rehabilitation officer and the office of the National Assistance Board. The student reports his findings to a group which includes other students, the medical registrar, the chief almoner and the senior lecturer in social and preventive medicine.

Later on when the students are working in the special departments they have lectures on biostatistics, and on the care of the handicapped and disabled. A morning is spent with a district nurse, a health visitor or a public health inspector and a visit paid to a factory and the hospital's occupational therapy department. At this stage small groups carry out elementary epidemiological surveys. More instruction is given during their final year while they are working in the paediatric department: there are tutorials on neglected children, illegitimacy and juvenile delinquency: visits are paid to a special school, a day nursery and a children's home. It is, also, during his last year that the student can opt to spend an evening a week for 3 months with a general practitioner or spend a fortnight full time with one.

The point is made that this type of teaching social medicine cannot be safely left to the clinical teachers alone and that if someone concentrates on it the teaching will not be neglected.

In a section headed "Future Developments" the suggestion is made that the social sciences are becoming more important in the teaching of medical subjects and that they might find a place in the preclinical period. It is, also, suggested that more attention should be paid during the time that pre-registration appointments are being held to the social problems presented by the patients.

The paper concludes with the report of a Social Medicine Case Conference written by a medical student.

Allen Daley

BRITISH MED. STUDENTS' ASS. **Report on the Teaching of Social Medicine in British Medical Schools** [MACSWEEN, R. N. M., Education Officer 1958–59 (prepared by)]. 23 pp. [? 1961.]

This report is based on information obtained from 14 medical schools: 6 in London, 4 in English provincial universities, 3 in Scotland and 1 each in Wales and Northern Ireland. 3 have no regular course in social medicine, the other 11 have courses of lectures which vary in number from 10 in the West London School to 60 in Aberdeen together with visits to places of public health interest.

The opinions of the students were "that social medicine ought to be taught as an individual subject"; not, however, in great detail but sufficiently to give an insight into "Epidemiology, Sociology, and the Administrative and Auxiliary Service of the National Health Service."

The recommendations are that "in all schools a course of social medicine should be included as part of the teaching in undergraduate medicine"; that the course "should serve to give an insight into those aspects which will be of immediate concern to the newly qualified doctor" and include "(a) Medical Sociology. (b) Epidemiology. (c) Public Health Administration. (d) The Health and Welfare Services."

Social medicine should not, however, be included as a subject in the final examinations but a tentative suggestion is made that there might be a combined examination in social medicine and infectious diseases. Visits should be arranged to factories, kitchens (for large scale preparation of food), special clinics and to patients' homes with health visitors or almoners.

[To all who wish the newly qualified doctor to have knowledge of preventive and social medicine any account of the present position will make sorry reading.]

Allen Daley

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. No. 212. **The Use and Training of Auxiliary Personnel in Medicine, Nursing, Midwifery and Sanitation. Ninth Report of the Expert Committee on Professional and Technical Education of Medical and Auxiliary Personnel. Geneva, 19–23 September 1960.** 26 pp. [11 refs.] 1961. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

The auxiliary worker is defined as a technical worker in a particular field who has less than the full professional qualifications. The term includes medical assistants, assistant nurses, assistant midwives, and assistant health inspectors. The need for these types of workers in the medical field arises from the increasing demand for auxiliary services particularly in relation to geriatrics, chronic illness, and rehabilitation in the developed countries, and from the desire for quick development of health services in the developing countries. In both types of country it is necessary to economize on training requirements partly because the required number of people with suitable educational background are not available for full professional training, and partly because it is uneconomic to employ highly trained people to do tasks which can be done equally well by people with less training.

It is necessary to appoint a director of education and training of auxiliary medical personnel to supervise the training programmes in the area, to approve training courses, and maintain contact with all the teachers. He should not be a dictator of policy. The auxiliaries must have appropriate recognition and support and their conditions of service should be such that they have an appropriate status in the community, and among other professional workers. It may be necessary to avoid the term "assistant" in describing the status of these workers. There should also be an incremental salary scale with adequate promotion prospects and possibilities of advancement with further training to the professional grades.

In selection, attention must be paid to the health, initiative, self-reliance, expressed interest, and reliability of the candidates. Educational attainments should be the minimum required for the assimilation of the technical knowledge and instruction given. A short probationary period should be introduced as part of the selection process. In general the needs of many

countries can be met by multi-purpose auxiliaries working with the three broad groups of professional workers in (1) curative medicine, (2) nursing and midwifery and (3) environmental sanitation. These multi-purpose auxiliaries may have to be supplemented with single-purpose workers as indicated by local requirements.

The auxiliaries must be trained to appreciate and take into account in their work the social and cultural patterns of the community in which they are working. They must know how to enlist and how to receive the co-operation of the community. They must be willing to assist in all activities related to the general health and welfare of the community, and they must be prepared to give first-aid and emergency medical treatment as in some areas they will be the only representatives of the medical services who are readily available. The training has to integrate theory with practice and inculcate the team concept. The material of any syllabus must be presented in a logical order throughout the course, the aim must be the development of the critical approach and of the student's personality. The content should include further practice in the use of the language of instruction or of the language that is in common use in the communities in which the person will work. The background of the relative basic sciences, the theory and technical skills of those subjects relevant to each category of function of the auxiliary, the accurate keeping of records, the care of equipment and stores, some instruction in administrative and personnel management and, as has already been mentioned, a knowledge and ability to render first-aid and emergency medical treatment should be kept in mind. On completion of training the student should pass a regulated examination conferring a recognized status on him. The location of the training schools should be on the outskirts of provincial or regional towns rather than near the larger national institutes of cities.

Teachers of the auxiliaries must not only be competent within their own field of work, but also have considerable experience and knowledge of the art of teaching, more so in fact than is needed for university teachers.

Currently with the training of the auxiliaries, it is necessary to obtain the understanding and co-operation of the professional groups under whom the auxiliaries are to work. After training, arrangements must be made for the supervision and follow-up of the auxiliaries so that the appropriateness of their training can be evaluated. *M. D. Warren*

OSAKA PUB. HEALTH ASS. BUREAU OF INTERNAT. FRIENDSHIP. **Public Health Administration in Osaka.** 27 pp., 2 charts. 1959. Osaka: 45–5 Koraibashi, Higashi-ku, Japan.

The Osaka area is divided into the "Administrative City District" (Osaka city and Sakai city) and the "Prefectural District". Osaka city has its own health department, Sakai city its own health centre under the control of the city administration. In the Prefectural District there is a health centre for each 100,000 or more of the population. In each health centre there are 3 sections (management, sanitation and preventive medicine), and in 3 there is a further section for information and education. The staff are all full-time; there is a shortage in all grades. Since 1957 scholarships have been available to medical students on condition that they enter the public health service on graduation.

The population in the whole area was 4,837,871 in 1956. The birth rate was about 27 per 1,000 between 1928 and 1943, it then rose in the period 1947–1949, but thereafter declined sharply to 15 per 1,000. This decline can be attributed to the prevalence of artificially induced abortions, popularization of birth control and the decrease in marriages. The number of reported artificial abortions in 1956 was 65,701 compared to 75,477 live births. The crude death rate in 1957 was 7·2, and the infant mortality rate was 35·4 per 1,000 live births, having been 79·9 in 1947. The leading causes of death are vascular lesions of the central nervous system, cancer, senility, heart disease and tuberculosis. Pneumonia and bronchitis, accidents and suicide are the next three commonest causes of death.

The prevalence of tuberculosis is high and the control of this disease has been the main activity of the health centres. Measures taken include prophylaxis, treatment and patient supervision. The chiefs of all establishments including schools and business offices, must have their staff examined once a year. All schoolchildren and all who are not employed must also be examined at the health centre, the remainder being examined by special organizations under the supervision of the health centre. Since 1957, the examination has been free, but even so only about 30% of the general population are examined each year. The cost of treatment to the patient is usually very small, because various funds contribute to the cost. All cases of tuberculosis must be notified. Patients treated at home are visited by public health nurses who advise about treatment and prevention of family infection.

Each pregnancy must be reported to the local health authority. The pregnant woman is given the necessary antenatal care and advice. Health examinations of infants and children are carried out, and treatment is given to children who are physically handicapped or who may become handicapped. Prematurity must also be notified, and prompt care is instituted for the baby.

Eleven diseases are notifiable—dysentery, typhoid, paratyphoid, cholera, typhus, smallpox, scarlet fever, diphtheria, meningitis, encephalitis and plague. Any patient with one of these diseases must be admitted to hospital and isolated and his home disinfected by the local health authority. In addition cases of influenza, rabies, tetanus, infectious diarrhoea, whooping cough, measles, acute poliomyelitis, malaria, filariasis, yellow fever, anthrax, tsutsugamushi disease and relapsing fever must be reported. The incidence of diphtheria and typhoid are high compared with many countries, while the number of cases of measles reported is low. Immunization against smallpox, diphtheria, whooping cough, typhoid and paratyphoid is compulsory.

84% of the Osaka prefecture is supplied by water systems; but less than one-half of the sewage is treated in disposal plants. Some of the remainder is used as

fertilizer and some is dumped, without treatment, in the bay.

The work of sanitation inspection needs to be developed. The work is divided into 3 sections, the supervision and issuing of licences for various premises, the supervision of the disposal of garbage and night-soil and the supervision of rodent and insect control. Food inspection is carried out by specially selected graduates of pharmacology and veterinary science.

Hookworm infestation is as high as 35% in the most infected regions. The incidence of notified venereal disease has dropped considerably since the introduction of the anti-prostitution law, but it is believed that the prostitutes have gone underground and that there is a possibility that the incidence of venereal disease is increasing. Three-quarters of the patients in mental institutions are suffering from schizophrenia. There is, as yet, no administrative programme to prevent chronic non-infectious diseases nor to rehabilitate patients suffering from such diseases; but a start has been made in conducting some routine medical examinations. *M. D. Warren*

Osaka Pub. Health Ass. Bureau of Internat. Friendship. **The Service of Health Centers in Osaka.** *O.P.H.A. Ser. No. 2.* 1960, 20 pp., 2 charts & 11 figs. on 4 pls. Osaka: 45–5 Koraibashi, Higashi-ku, Japan.

Each health centre in Osaka supervises the health services of its district and serves between 150,000 and 200,000 people. The work is divided into 3 sections, Management, Sanitation and Preventive Health. In the future, it will be necessary for some health centres to provide additional services, especially of a curative nature, in rural areas. The present work includes routine examinations for the detection of patients with tuberculosis, BCG and other inoculations, services for maternity and child welfare including birth control education, environmental sanitation, supervision of food hygiene and at some selected health centres routine examinations for the early detection of cardio-vascular disease and of uterine cancer are carried out. *M. D. Warren*

Osaka Prefectural Govt. Health Dept. **Public Health Research Center in Osaka.** 10 pp., 1 fig. 1960.

Osaka Prefecture established a Public Health Research Centre in 1960. The research work to be carried out will include investigation into the pollution of Osaka Bay, industrial fatigue, methods of qualitative and quantitative chemical analysis of industrial environments, industrial management, causes of mental illness and suicides, and other matters relating to public health. *M. D. Warren*

De Grazia, G. L'organizzazione sanitaria nell'U.R.S.S. [**Health Organization in the USSR**] *Ann. d. San. Pubblica.* Rome. 1961, Jan.–Feb., v. 22, No. 1, 3–36, 7 diagrams.

VITAL STATISTICS

Alison, F. & Corone. Les subdivisions de la mortalité foeto-infantile (1957–1958–1959). [**Subdivisions of the Total Infant Death Rates in 1957–1959**] *Bull. Inst. Nat. Hyg.* Paris. 1961, Mar.–Apr., v. 16, No. 2, 371–89, 10 maps.

The infant mortality in France has continued to fall and, as in other countries, the largest improvement in the rate has occurred after the first month of life; the smallest reductions were stillbirths and the deaths in the first week of life. Infant mortality has been examined in sub-divisions, stillbirths, deaths in the first week of life, perinatal deaths, neonatal deaths, and deaths in the first year of life plus stillbirths. These rates are given for each of the 90 Departments of the country for 1952–55 and 1957–59. The ratio of perinatal mortality to infant mortality plus stillbirths and the percentage difference between the rates for the two periods has been found. The geographical variations in the size of the rates are considerable. For the country as a whole the perinatal rate fell from 35·3 in 1952–55 to 32·3 in 1957–59, the neonatal rate fell from 17·2 to 13·8 during this period and the total infant death rate, including stillbirths, from 60 to 48·5. *W. J. Martin*

Mazer, A. Sevrage et mortalité infantile en pays Lobi. [**Weaning and Infant Mortality in the Lobi Area, Upper Volta, West Africa**] *Bull. Inst. Nat. Hyg.* Paris. 1961, Jan.–Feb., v. 16, No. 1, 127–37, 1 graph. [18 refs.]

An enquiry is reported covering 1,084 married women, living in 21 villages in the Upper Volta region, who gave birth to 4,528 children during the period of the investigation. The infant mortality rate was 128 per 1,000. During the age period 1–3 years, 183 per 1,000 of the original group died, a remarkably high mortality. The critical point was at 2 years; if the child passed this point, its chances of survival were relatively good. Mortality between 1 and 2 was closely related to the time of weaning. In children weaned before the age of 10 months, the mortality between 1 and 2 years reached 50%. The main cause of early weaning was a further pregnancy.

On weaning the children were fed mainly on preparations of millet or maize, in the form of "cakes" or gruels, sources of animal protein such as milk and meat being absent from their diets. The author comments that these preparations are unsuitable for children under 2 years of age, failing to satisfy requirements

for protein and certain vitamins during the period of rapid growth, but that they became more satisfactory in these respects when taken by older children.

The whole picture presented in this paper, with its emphasis on the vulnerability of children to malnutrition during the weaning and post-weaning periods, is common to many countries in Africa and elsewhere in the tropics and sub-tropics. *W. R. Aykroyd*

EPIDEMIOLOGY

ANDERS, W. & MEIER, E. Epidemiologische Jahresübersicht 1958 für das Bundesgebiet und West-Berlin. [**Epidemiological Annual Report for 1958 for the Federal Republic of Germany and West-Berlin**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 3, 285–344, 24 figs.

This official report contains much information with many tables, maps and figures on the incidence of transmissible diseases in the Federal Republic of Germany and West Berlin in 1958. The experience of tuberculosis is, however, excluded. In general 1958 showed a considerable reduction in the numbers of recorded infections.

Enteric fever in the Republic was somewhat reduced from 2,144 cases or 0·42 per 10,000 inhabitants in 1956 to 1,690 cases or 0·32 per 10,000 in 1958. Maps show the varying incidence in different areas of the country. No important reduction in incidence occurred in West Berlin.

Paratyphoid fever showed a fairly satisfactory reduction in numbers. The incidence of bacterial food poisoning due mainly to salmonella infections was halved in 1958 (2,280 cases) as compared with 1956 (4,442 cases) in the Republic but in West Berlin had increased from 124 cases in 1956 to 223 in 1958.

Bacillary dysentery is considered at some length and there has been but little change in incidence—2,274 cases in 1958 (0·43 per 10,000) and 2,506 in 1956 in the Republic although in West Berlin there was a considerable improvement. A table which illustrates for comparison the recorded incidence in other countries gives for England and Wales in 1958 the figures of 42,002 cases, a morbidity rate of 9·31 per 10,000.

Scarlet fever incidence remained high at over 30,000 cases; the numbers of diphtheria cases was reduced from 8,280 in 1956 to 5,130 in 1958 in the Republic but there was an increase from 119 to 306 cases in West Berlin; and some lessening of whooping cough from nearly 39,000 to 31,000 cases in the Republic.

Short accounts are given of the incidence of brucellosis, "epidemic" meningitis, tularaemia, leprosy, anthrax, Weil's disease, rabies, trachoma, psittacosis, malaria, trichinosis and influenza. Poliomyelitis (1,556 cases in the Republic and 194 in West Berlin in 1958) is considered at greater length, with comparison of the experience with that of other countries and some description of the amount of active immunization which has been carried out in the Federal Republic.

Infective hepatitis which is not universally notifiable presents a problem, particularly in certain areas of the country such as Bavaria (2,612 cases in 1958) and Hamburg (996 cases in 1958).

The occurrence of a small epidemic of 19 cases of smallpox with 2 deaths in Heidelberg is described. The infection was introduced by a doctor who had been visiting India. *M. E. Delafield*

SARMENTO, A. Aspectos e evolução da mortalidade no arquipélago de Cabo Verde. [**Trends in Mortality in the Cape Verde Islands**] *Anais Inst. Med. Trop.* Lisbon. 1959, Jan.–Dec., v. 16, Nos. 1/4, 229–66, 2 charts (1 folding). [20 refs.] English summary.

At the census of 1950 the population of these islands numbered 148,331; the estimated population for 1954 was 167,694. A table shows that general mortality rates varied from 20·3 to 27·9 per 1,000 (1931–39), 19·1 to 37·3 (1940–49) and 12·4 to 17·8 (1950–56) except for two major peaks, 75·7–107·1 in 1941–42 and 81·3–107·9 in 1947–48, when failure of the rains resulted in famine. The recent trend has been quite sharply downwards.

The author deals *seriatim* with the main groups of causes of death. Respiratory tuberculosis fell to 59·3 per 100,000 in 1955 though BCG was introduced only in 1956. Syphilis and its sequelae have remained fairly constant in the period 1950–55, and the same is true of typhoid fever and dysentery. Mortality from diphtheria was slight, but whooping cough deaths rose from nil in 1952 to 74·3 per 100,000 in 1953 and 200·9 in 1954. There was an epidemic of cerebrospinal fever in 1951–52.

No deaths were registered from poliomyelitis in 1950–55 but smallpox accounted for a sharp peak of 56·7 per 100,000 in 1951, and measles for a peak of 100·1 in 1954. Malaria was still prevalent as one of the leading causes of death—288·1 per 100,000 in 1950; 81·9 in 1955.

The death rates for malignant growths were not as high as in many European countries, nor were the rates for vascular lesions of the central nervous system, and the rates for arteriosclerotic and degenerative lesions of the heart at 0.5–7·6 were much below the rate for Portugal (114·3), though diseases of the cardiovascular system averaged 79·9. Pneumonia was a fluctuating cause rising to 177·5 in 1954, and the intestinal infective diseases (excluding the newborn) rose to 265·3 in 1953. Other diseases of infancy and prematurity accounted for 148·5–335·0 per 100,000 in 1950–55, and senility for 139·9–425·7.

Infant mortality at 542·9 per 1,000 live births in 1947 (the year of famine) fell to 130·7 in 1950, but the rates have not fallen much since the early years of the century; they represent almost one-quarter of the total deaths.

The author sums up the 3 major needs:—(1) to increase the (insufficient) number of doctors and sanitary personnel; (2) to institute an intensive campaign for the protection of mothers and infants; (3) to combat the principal endemic diseases.

Charles Wilcocks

LEMON, F. R. **Health Problems of the Navajos in Monument Valley, Utah.** *Pub. Health Rep.* Wash. 1960, Nov., v. 75, No. 11, 1055–61, 1 chart. [13 refs.]

The author and his colleagues carried out a survey in 1956–58 during which information was collected on vital statistics and certain diseases. The Navajo population shows a higher proportion of children and a lower proportion of adults than the United States as a whole, and the infant mortality seems to be about 3 times as high in the Navajos as in the United States as a whole. The picture is of high birth rate and high rates of infant and child mortality [which is what one would expect in a relatively backward community], but the mortality rates are falling as the medical facilities are being more freely used.

Tuberculin tests (0·0001 mgm. PPD) on 967 persons showed positive rates rising to 64·5 at age 20–29, and 87·2% at age 50 and over. 5 of 373 persons tested with histoplasmin were positive, and 23 of 469 tested with coccidioidin [figures in tables and text do not correspond].

The major diseases of this rather isolated group include tuberculosis and other respiratory, gastro-intestinal and miscellaneous infections. Their way of life is insanitary, and their health practices and attitudes continue to be influenced by ancient cultural concepts. As a result of the present investigation it is believed that "a crude baseline for the health status of Navajos in the region has been ascertained".

Charles Wilcocks

MATERNAL AND CHILD HEALTH

MARTIN, G. K. & LADD, K. B. **Maternal and Child Health Services, Ontario, 1958.** *Canadian J. Pub. Health.* 1961, Mar., v. 52, No. 3, 111–19.

The authors are the Director of Public Health Administration and the Statistician of the Maternal and Child Health Branch of the provincial government of Ontario. In this province local health services are the responsibility of the autonomous boards of health. The paper presents the findings of an enquiry made in 1958 into the work done in the 33 health units and the 14 health departments employing a full time medical officer of health. Each area was visited for, at least, one half day and a questionnaire, including statistics, was completed.

The subjects covered were: Population data: Prenatal programme: (a) home visits (b) prenatal classes ; Postnatal and infant programme: (a) hospital visits to the mother (b) home visits to mother and child (c) child health conferences and clinics; School health programme: medical and nursing programme in (a) elementary and (b) secondary schools.

The population of the 47 agencies included in the survey was 4,279,000 which is 76% of that of the province. The overall crude birth rate was 26·0 per 1,000 population.

The number of expectant mothers visited at home was small (about 13%) and in only 3 areas did it exceed 30%: 30 of the 47 areas provided official prenatal classes and in 3 others the Victorian Order of Nurses (District Nurses) held classes. Nurses of the Order also assisted in several of the local authority classes. A public health nurse was responsible for the operation of the classes in all cases but in 8 a doctor and in 6 a nutritionist undertook part of the teaching. The length of each course was 8 to 10 sessions. The percentage of expectant mothers taking advantage of them was less than 5.

The postnatal visiting programme is handicapped by the lack of any scheme for the notification of births to the local health department. In most areas the public health nurse calls at the local hospital to obtain particulars of the births and on the local Registrar of Births but the former source of information is incomplete as so many mothers go for their confinements to hospitals outside their area of residence. Nevertheless, a substantial proportion were visited within the first 2 weeks of life. In practically all the 47 areas there was either a child health clinic (a doctor present) or a child health conference (a public health nurse only). In 36, immunizations were done at the centre. The average attendances per session were 33 at the clinics and 9 at the conferences.

In 45 areas the local health authorities, as distinct from the education authorities, had sole responsibility for the school health programme. In most it was their major activity.

In only 12 of the elementary school areas were all medical examinations carried out by doctors employed by the authority: in the rest the parents were encouraged to have the medical examination on entrance to school made by the family doctor and it was usual for more than half the parents to arrange (and presumably pay for) this. Routine medical examinations in later school life are being dropped but children are presented by the school nurse if anything amiss is

noticed. Public health nurses test the vision in 35 areas and in the rest other nurses or teachers do it. Audiometric testing of hearing is replacing cruder methods.

In the secondary schools there are more routine medical inspections than in the elementary, and those scholars engaged in "body contact sports" receive special attention. The school health service is the largest consumer of the time of the public health nurses.

[It will be observed that there are several fundamental differences between the above and the normal British service.] *Allen Daley*

VARANGOT, M. J. La prévention de la mortalité et de la morbidité foetale dues au traumatisme de naissance. (Etude comparative de deux séries de 10,000 accouchements). **[Prevention of Foetal Mortality and Morbidity due to Birth Injury]** *Bull. Acad. Nat. Méd.* 1961, v. 145, Nos. 9/10/11, 242–6.

Although the cause cannot be established with any certainty in many neonatal deaths the author suggests that a reduction in the death rate can be affected by reducing the number of deaths due to injury at birth. The term injury has been used in a wide sense and includes besides injuries, such conditions as anoxaemia in the infant and deaths due to difficulties in uterine contractions in the mother. In recent years dystocia has been treated with intravenous injection of oxytocin; resort has been made more frequently to episiotomy to shorten the duration of the period of expulsion and an improved technique has been introduced for resuscitation. The death rate per 100,000 deliveries in the Maternité de Port-Royal during 1946–49 was 264 and during 1954–59 it was 176. Infants dying before labour numbered 91 and during labour 147 in the first period and 103 and 53, respectively, in the second period. Extraction by forceps fell from 692 to 598 and caesarian section rose from 386 to 412 between the 2 periods. Episiotomies increased from 563 in the first period to 2,462 in the second period. Babies requiring resuscitation were 247 fewer in the second period and on the average they required a shorter spell of treatment.

The author concludes that although simple techniques will reduce the death rate from birth injuries a high standard of skill and care is necessary during labour. *W. J. Martin*

HEALTH OF OLD PERSONS AND THE CHRONICALLY ILL

RADFORD, J. G. **Management of the Aged Patient.** *Med. J. Australia.* 1961, Mar. 11, v. 1, No. 10, 362–6.

The "aged patient" is defined as a person who "is physically or mentally incapable of contributing usefully to the common good, or is likely to be requiring supportive help of some description" from his doctor or ancillary services. In Australia 5% of the population are old-age pensioners; in New South Wales, there are twice as many women to men in this group and over one-third of the old-age pensioners are 75 years or older.

Most patients would prefer to be cared for, in their declining days, in their own or a relative's home, although modern houses often lack sufficient space to enable the relatives to cope. For those elderly persons who prefer to be independent, such additional help as "meals on wheels" and visiting social workers are a great help, but are sadly lacking in Australia. The provision of institutional care is largely a matter of private enterprise; the few state homes having long waiting lists.

The pensioner medical service is of the greatest value. The doctor working in the scheme must have the ability to deal with the patient, his family and his social surroundings. The clinical conditions met with are headed by the circulatory conditions (arteriosclerotic and hypertensive disease) and then osteoarthritis, respiratory disease, digestive disorders (peptic ulcers and diverticulitis), psychiatric disorders, diseases of the skin, diabetes, hypothyroidism and cancer. Some of the conditions are peculiar to old age, some occur at all ages and some which are more common in youth turn up in an atypical form in older age.

In treating the "aged patient" a proper clinical appraisal is as necessary as a careful assessment of the social conditions. The family doctor is the person to do this. At both undergraduate and immediate postgraduate level there is a need for further education in the social and clinical implications of caring for aged people. *M. D. Warren*

See also p. 771, UNITED STATES DEPT. HEALTH, EDUCATION & WELFARE, **Infectious Diseases in the Aging. 1961 White House Conference Edition.**

CHRONIC CARDIO-RESPIRATORY DISEASES

MORRIS, J. N., CRAWFORD, M. D. & HEADY, J. A. **Hardness of Local Water-Supplies and Mortality from Cardiovascular Disease.** *Lancet.* 1961, Apr. 22, 860–62. [18 refs.]

Correlations have been calculated between indices of hardness of the local water and the death rates (1948–54) from different causes in the 83 country boroughs of England and Wales. The results at ages 45–74 show a considerable and *inverse* degree of association between hardness and cardiovascular disease (coefficients of the order of −0·5) but only small and insignificant associations with non-cardiovascular causes of death (the main exception is bronchitis with its several connexions with heart disease). Within the cardiovascular group the correlations are substantial for deaths from vascular lesions of the nervous system and for those certified to "myocardial degeneration"; in coronary heart disease the correlation is sizeable only in middle-aged men; correlations with mortality certified to hypertension and other cardiovascular causes are not remarkable.

It does not appear that the association is merely regional—soft water supplies and cardiovascular mortality happening to go together—and there is no significant association between water hardness and the other local social indices explored, such as population density, social class composition, infant mortality, etc. Analysis by constituents of the water shows a high correlation between the cardiovascular death rate and the calcium content, none with the magnesium content and very little, if any, with sulphate content. Clearly there is a case for much further work and this is under way. *A. Bradford Hill*

See also p. 738, WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 213. **Chronic Cor Pulmonale. Report of an Expert Committee. Geneva, 10–15 October 1960.**

CANCER

BOUCOT, Katharine R., COOPER, D. A. & WEISS, W. **The Philadelphia Pulmonary Neoplasm Research Project: an Interim Report.** *Ann. Intern. Med.* 1961, Mar., v. 54, No. 3, 363–78, 1 fig.

Between 1951 and 1955 every man aged 45 or over who presented himself for a chest X-ray at the Central Unit of the Philadelphia Tuberculosis and Health Association was invited to join this Project and to report twice a year for an X-ray and questioning about any symptoms. 6,137 were enrolled and have been followed up, at the time of the present report, for 3½ to 7½ years. [The completeness of the follow-up is not specified.] In 66 of these men lung cancer was identified at entry, in 26 it has subsequently developed. 8 of these 26 men were asymptomatic at entry, had had no X-ray evidence of cancer at that time, even on special retrospective review, and had attended regularly. Clinical details are set out to show the development of their carcinoma. They show that symptoms preceded X-ray changes by many months in 2, were concurrent in 2 and followed the X-ray changes by as long as 9 and 24 months in the remaining 2. Relating the smoking habits of the 92 lung cancer cases to the habits of the total 6,137 men shows a distinct association. Only 1 cancer, an undifferentiated carcinoma with some unusual sarcomatous characteristics, was found among the 806 non-smokers (0·12%) compared with 91 cases in the 5,331 smokers (1·7%) and 24 in the 978 smokers of more than 1 pack of cigarettes daily (2·5%). *A. Bradford Hill*

KISSEN, D. M. & EYSENCK, H. J. **Personality and Lung Cancer.** [Correspondence.] *Brit. Med. J.* 1961, Apr. 15, 1107.

In a previous paper [this *Bulletin*, 1960, v. 35, 840] it was reported that a study of smoking and personality supported the hypothesis that genotypic personality differences are related to smoking habits. The cigarette smokers were significantly more extroverted and less rigid than non-smokers; it was expected that they would be more neurotic but they were not found to be so. These results, it was concluded, "do not prove that smoking does not cause lung cancer but they make more reasonable than had previously been the case the proposition that both smoking and cancer may be causally related to certain underlying genotypic factors. Perhaps the most appealing hypothesis is that extroverts live at an accelerated rate, drinking harder, smoking harder, living more irregular lives, staying up longer, and generally 'living it up' more. They may thus (a) lower their resistance to disease, and (b) expose themselves more to conditions which may directly cause the disease in question. . . . a direct study should be undertaken of the personality of victims of lung cancer; if they could be shown to be more extroverted than a carefully chosen control group the theory here advanced would receive considerable support."

This direct study has now been undertaken, it is briefly reported in this letter and it gives no support whatever to the theory. The 116 lung cancer patients

are not appreciably or significantly more extroverted than the 123 control patients and, contrary to expectation, they have significantly *less* neuroticism.

A Bradford Hill

VOELCKEL, J. & BLACHÉ, R. Note sur le cancer au Sud-Cameroun. **[Cancer in the South Cameroons]** *Méd. Trop.* Marseilles. 1961, Mar.–Apr., v. 21, No. 2, 141–4, 1 graph.

DENTAL HEALTH

TANK, Gertrude & STORVICK, Clara A. **Dental Caries Experience of School Children in Corvallis, Oregon, after 7 Years of Fluoridation of Water.** *J. Pediatrics.* St. Louis. 1961, Apr., v. 58, No. 4, 528–37, 2 figs. [24 refs.]

The purpose of this study was to investigate the effect of 7 years of fluoridation of water on the teeth of schoolchildren in Corvallis, Oregon. Fluoridation was begun in January, 1953, when the natural amount of fluoride of 0·1 p.p.m. was adjusted to 1·0 p.p.m. by the addition of sodium fluoride in 1 plant and sodium silicofluoride in the other plant until 1957 when in both treatment plants only the silico-fluoride was used.

During November and December 1959, 1,129 Corvallis schoolchildren were examined and the findings compared with those, published in 1953, on dental caries in 1,534 Corvallis elementary schoolchildren. There is a description of the grouping of the children, the dental examinations, the symbols used to designate the dental caries experience and the statistical analyses of the results.

There is a clear account of the results of the study with discussion and a number of detailed tables and figures.

"The development of each permanent tooth covers a span of 10 years or more; therefore, a complete picture of the caries-inhibitory effect of fluoridation of water could not be observed after only 7 years", yet this study showed that 7 years of fluoridation has had beneficial results which are highly significant.

It was determined that the dental caries rates of the permanent and primary teeth for children of ages 5 to 12 years were significantly reduced by 7 years of exposure to fluoridated water. A marked reduction in caries incidence also occurred in teeth which had developed before fluoridation was instituted. Among other results given in the summary are:— (1) "A significant reduction was shown in the number of decayed and missing permanent teeth, decayed primary teeth, and teeth indicated for extraction", (2) "A marked increase in the number of filled permanent and primary teeth after fluoridation compared to the prefluoridation data" and (3) "After fluoridation, more than twice as many children were free from caries experience of the permanent or primary teeth as had been before fluoridation".

M. E. Delafield

MENTAL HEALTH

LAMBO, T. A. **Further Neuropsychiatric Observations in Nigeria with Comments on the Need for Epidemiological Study in Africa.** *Brit. Med. J.* 1960, Dec. 10, 1696–704. [28 refs.]

In this paper the author, who is a specialist psychiatrist in the Western Region of Nigeria, comments in clear and serious prose on the common mental disorders of the area, with particular emphasis on the cultural background of the patients. For instance, for the psychoses the most vulnerable class of the population is the African student class, who have their own mental health problems at home and abroad. In Africa the prognosis of mental illness is good, and this is probably because the "favourable social and environment factors inherent in the community to which the mentally ill are exposed in Africa influence the threshold of incapacity". Witchcraft, supernaturalism and attempted suicide are more common among detribalized, urban Africans than among those living more traditional lives.

"Most of the major psychoses and psychoneuroses have been seen. Others have been encountered which seem peculiar to Africa, and the clinical fact remains, and supports the view, that most of these do not fit into the existing nosological framework but are nevertheless susceptible to interpretation in terms of observable cultural factors."

The author concludes this thoughtful article as follows:—

"Our present clinical observations in Africa have shown that, although in mental illness there may be some essentially basic factor in the onset of the illness (in endogenous psychoses, for example, the constitutional and genetic factors may be the *sine qua non* of their inception), yet the interplay between man and his physical and social environment would seem to influence considerably the evolution of the disorder—that is, its property of remaining latent or manifest, its later course, and its final outcome.

"It must be emphasized that for a truly scientific understanding of human behaviour, especially that aspect of medicine relating to human ecology, man has to be studied at various stages of his social evolution—that is, at different times, in different cultures, and under various circumstances."

Charles Wilcocks

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution Port, Ship and Aviation Hygiene.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

CROWDY, J. P. **Pure Water from Foul.** *J. Roy. Army Med. Corps.* 1961, Apr., v. 107, No. 2, 64–8.

The provision of a safe drinking water in times of nuclear warfare would pose hitherto unexperienced problems, and counsels of perfection would probably be impracticable. Water supplies would be so scarce that it would be essential to accept almost any source available. Bearing these facts in mind, the author sought the most polluted water he could find. In the River Blackwater where it flows from Camberley to Sandhurst Village, he found such a water, characterized by an abundance of *Escherichia coli* and a high ammoniacal and albuminoid ammonia concentration.

In the summer of 1959, tests were carried out on this water to assess the effectiveness of the 3,000 gallons per hour service-pattern mobile water purification plant at present in use. Parts of these trials to produce a potable water by stellar filtration and electrolytic chlorine are described in detail. Bacteriological examination was confined to the coliform count and an agar plate count after 24 hours at 37°C. The Ministry of Health (1957) standard multiple tube method was used in the coliform test, and a representative selection of positive tubes were subcultured at 44°C. to confirm the organisms as *E. coli* I.

The results of these trials show that in 15 minutes a potable water was produced in all samples having an initial chloramine concentration of 3·7 p.p.m. or over. Further contact did not increase the bactericidal action, a finding at variance with standard military teaching which has always stressed the necessity for contact of at least one hour. In the equipment tested, the chlorine is produced by electrolysis of brine, and in waters having a high ammonia content, the chlorine produced was exclusively chloramine. It would appear from the results obtained that the swift bactericidal action is due to the action of free chlorine before it can combine with the ammonia.

It may be concluded that a chlorine residual of 4 p.p.m. of whatever composition together with stellar filtration will produce a safe potable water in 15 minutes, however polluted the source. *E. Windle Taylor*

LENK, V. & ACKERMANN, H. W. Erfahrungen über die Isolierung von Typhus Vi- und Salmonellaphagen aus Fluss- und Abwasser. **[Experiences concerning the Isolation of Typhoid Vi and *Salmonella* Phages from Surface Water and Sewage]** *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 2, 224–33, 3 figs. [25 refs.]

The investigation of typhoid Vi and salmonella O phage content of a water sample can be useful in estimating its hygienic quality. The authors found however that the isolation and identification of specific typhoid Vi phages involved technical difficulties which rendered the method unsuitable for large scale routine investigations. The isolation of pure Vi phage strains involved a considerable expenditure of time. Samples of Berlin surface water were investigated for their Vi phage content, salmonella O phage content and for salmonellae present. The findings showed, on comparison of plate count, *coli* titre, salmonella count and salmonella O phage content, an interesting correlation between *coli* titre and salmonella phage content. The isolation of salmonella phage indicates the presence of faecal pollution. The phage content and the salmonella count could only be related occasionally.

E. Windle Taylor

SKOUGSTAD, M. W. & FISHMAN, M. J. **Water Analysis.** *Analytical Chemistry.* 1961, Apr., v. 33, No. 5, 138R–164R. [Numerous refs.]

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

WAGNER, E. G. & LANOIX, J. N. **Excreta Disposal for Rural Areas and Small Communities.** *World Health Organization Monograph Series No. 39.* 187 pp., 73 figs. [46 refs.] 1958. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [25s.; $5.00; Sw.fr. 15.–.]

It is conclusively demonstrated in the opening pages of this book that faecal-borne diseases in tropical countries are responsible for a high morbidity and mortality and for economic losses of staggering proportions. Indeed, in under-developed areas "it would be possible to amortize within a period of five years the cost of rural sanitation facilities from the savings which would accrue from the reductions in typhoid fever, diarrhoea and enteritis".

After the introduction, the book consists of 4 sections.

The first shows the public health importance of excreta disposal, and the social and psychological implications of rural sanitation programmes. This is followed by a long section on the privy method of disposal which includes all the methods most suitable for introduction in the rural areas of developing countries. It deals with factors influencing design, the evaluation of different systems and the various forms of privy design. The next section deals with the septic tank and the disposal of effluent. The final section discusses the planning of excreta disposal programmes and the training and functions of the sanitation staff. There are 2 short annexes.

The book is by 2 public health engineers who write with obvious experience of the construction and maintenance of simple sanitary facilities. It is a thoroughly practical exposition of the ways of attacking the problem of rural excreta disposal in all its aspects. Compelling reasons are advanced favouring individual rather than public latrines and the objective of the book is the promotion of excreta disposal by the rural family. An anthropological approach to the subject is regarded as essential, and it is rightly stressed that irrespective of conditions some improvement can be made in every place. The book is generously illustrated with diagrams giving measurements. It will be of great value to health and public works staff concerned with rural sanitation. *T. H. Davey*

SEN, B. P. **High Rate Digestion of Liquid Wastes from Molasses Distillery.** *Alumni Ass. Bull.* Calcutta. 1960, Sept., v. 9, No. 16, 23–32, 4 figs.

The disposal of liquid wastes from distilleries presents an urgent and serious problem in the states of Bihar, Uttar Pradesh and West Bengal where molasses from cane sugar is the chief raw material used in the manufacture of industrial alcohol.

The characters of the wastes are described shortly and these are such that ordinary methods of treatment are not effective in reducing adequately the high BOD. Experiments were therefore carried out on anaerobic digestion and the results of these are here presented in some detail with tables and figures. Digestion in the thermophilic range gave no better results than at the mesophilic range and it was found that digested cowdung sludge is as efficient a seed as sewage sludge. The BOD of raw distillery waste digested for 40 days was reduced by 96–98%. Although the concentration of nitrogen in distillery waste is low it was found that the addition of nitrogen in the form of ammonium salts effected no improvement in digestion. Some work was done on the recirculation in the digesting waste of carbon dioxide present in the digester gas and it was shown that this resulted in a greater percentage removal of BOD and increased the percentage of methane in the digester gas. *M. E. Delafield*

ATMOSPHERIC POLLUTION

PHELPS, H. W., SOBEL, G. W. & FISHER, N. E. **Air Pollution Asthma among Military Personnel in Japan. Some of the Clinical Characteristics of this Disease and Therapeutic Measures that seem to give Patients most Relief.** *J. Amer. Med. Ass.* 1961, Mar. 18, v. 175, No. 11, 990–93.

In 1954 HUBER and co-workers reported "a new environmental respiratory disease which—at that time—was popularly termed Yokohama asthma" [this *Bulletin*, 1955, v. 30, 1088]. The present paper contains an account of the disease from an experience based on over 100 patients studied between September, 1959, and April, 1960. There is now evidence that the disease is not confined to the Yokohama area but involves the whole Kanto Plain. It is believed that the condition is caused by increased smog concentration from the high level of industrialization in the area.

The symptoms of coughing, wheezing and shortness of breath afflict otherwise normal, healthy persons in the 18–40-year age-group. Usually there is no family history of asthma, no history from the patient of significant allergy reactions and a "relatively unimportant psychological overlay is the rule."

Episodes of nocturnal coughing are the beginning and these may continue for days or weeks getting worse and leading to marked shortness of breath and chronic loss of sleep. Severe attacks are more frequent in the winter and during periods of increased smog concentration.

On leaving the Kanto Plain many of these patients promptly become asymptomatic although an "outstanding feature of this disease is its tendency to become chronic and progressive."

Extensive laboratory studies offered little guidance on treatment during acute attacks but most of the patients had evidence of marked air-flow obstruction even between attacks and while receiving medication.

In general the usual bronchodilators used for controlling asthmatic attacks were not really effective although some symptomatic relief was given by nebulized isoproterenol (Isuprel) hydrochloride and ephedrine given by mouth.

The treatment of severe cases of the disease is described in detail and there are some case reports. *M. E. Delafield*

AMDUR, Mary O. **Report on Tentative Ambient Air Standards for Sulfur Dioxide and Sulfuric Acid.** *Ann. Occup. Hyg.* London. 1961, Feb., v. 3, No. 2, 71–83. [Numerous refs.]

This report for the California Public Health Department discusses 10 conclusions derived from the literature on toxicology, and on them are based 3 unrelated sets

of standards intended for consideration and review in the control of atmospheric pollution. The third set is not for the oxidizing type of poilution characteristic of California, but represents values only for the reducing type, prevalent in Britain and Eastern American cities, during periods of meteorological inversion. The first 2 sets are presumably generally applicable, and should not be discounted because of higher threshold limits for industrial operation, a different matter. Particle size of mists and the presence of particulate matter have been taken into account. Damage to vegetation may need evaluation. In themselves, concentrations of sulphur dioxide and of the more toxic sulphuric acid, reported from average urban areas, do not constitute a public health hazard, when based on toxicological data, though epidemiological opinion may be different. The compounds were contributory but not causative factors in the 3 main world pollution disasters, and their importance to the general problem of air pollution lies in the response of sensitive individuals. The permissible average levels tentatively advocated have a wide safety margin to allow for such persons and for possible potentiating or synergistic effects.

In the table below concentrations which could produce effects in sensitive persons are termed adverse (causing sensory irritation), serious (altering bodily function or conducive to chronic disease), or emergency (likely to cause acute illness or death). Reasons are based on levels which have caused, *e.g.*, detection, symptoms, measurable bronchoconstriction in animals and healthy and sensitive human subjects, bronchospasm, etc.

Type of Standard	*Effect*	*Sulphur dioxide*	*Sulphuric acid*
		p.p.m.	mgm. per m.^{3}
1. For occasional peaks up to 1 hour	Adverse	5	1
	Serious	10	3
	Emergency	20	5
2. Permissible average levels	Nil	0·05	0·02
3. Only for reducing type pollution during inversion periods	Adverse	0·5	2
	Serious	1	4
	Emergency	2	8

M. Patricia Fitzsimons

CAPRIOGLIO, A. Inquinamento atmosferico da cemento: alterazioni polmonari nelle maestranze del cemento-amianto e nella popolazione. [**Air Pollution by Cement: Pulmonary Alterations among Asbestos-Cement Workers and among the Population**] *Rass. Med. Indust.* Rome. 1960, Sept.–Oct., v. 29, No. 5, 375–9. English summary (9 lines).

The general problem which is posed by the great quantities of dust given off in the cement and asbestos-cement industries is discussed and in particular that which has arisen in the town of Casale. The author is works doctor to a large cement works there in which all the workers and staff are submitted every year to routine screening and a clinical examination with special attention to the respiratory apparatus. As a result of these radiological examinations over a number of years an increased incidence of linear markings has been noted whether or not the workers were engaged in dusty work. Previous work is quoted to support the view that cement dust is not entirely innocuous and surveys by other observers have given similar results to those now reported.

It has been suggested by PARMEGGIANI that for health reasons the workers engaged on very dusty jobs change to other occupations and thus X-ray changes are distributed over a wide range of operatives. GRANDJEAN as a result of a statistical investigation found no substantial differences as regards affection of the respiratory organs between two groups of people respectively living in a place where a cement industry was established and in another without a works of this kind. In order to clarify the issue research was carried out which showed that the atmosphere was equally polluted by cement dust inside and outside the curtilage of the works. On X-ray examination dust changes were present in the population of the neighbourhood who had never worked in contact with cement materials or other dust. Similar X-ray lesions were found in the lungs both in people engaged in cement and asbestos-cement work and in the population in the district surrounding the works.

These results justify the suspicion that the atmosphere of this particular area of the town can be harmful to subjects particularly predisposed on account of various constitutional inherited or biological defects. Atmospheric pollution is an accompaniment of progress and a joint effort is urgently needed by the appropriate authority and by industrialists to reduce atmospheric pollution and thereby safeguard the health of the public which is seriously threatened.

[In the summary to this paper it is stated that 4,908 screenings were carried out during the years 1956–59, but the actual numbers concerned are not referred to in the text.] *G. F. Keatinge*

LODGE, J. P., Jr. **Air Pollution.** *Analytical Chemistry.* 1961, Apr., v. 33, No. 5, 3R–13R. [390 refs.]

LARSEN, R. I. **Parameters of Aerometric Measurements for Air Pollution Research.** *Amer. Indust. Hyg. Ass. J.* 1961, Apr., v. 22, No. 2, 97–101, 5 figs.

MUNN, R. E. **Air Pollution Control by Town Planning.** *Occupational Health Rev.* Ottawa. 1961, v. 13, No. 2, 13–16, 3 figs. [20 refs.]

PORT, SHIP AND AVIATION HYGIENE

COOK, P. B. **Marine Hygiene.** *J. Roy. Inst. Pub. Health & Hyg.* 1961, Feb., v. 24, No. 2, 31–41.

The author discusses the history of quarantine, and goes on to mention some of the important steps taken in the past to improve the health of seamen.

In discussing the situation of marine hygiene today, the author enumerates the minimum standards for crew accommodation, as laid down in the Merchant Shipping Crew Accommodation Regulations, 1953, and makes a passing reference to the importance of frequent deratting of ships. Social activities now include libraries, correspondence courses and facilities for improving both technical and general education. The efficacy of modern chemotherapy and antibiotics has reduced considerably venereal disease among seafarers but criticism is levelled at the poor organization of continuation treatment. Alcoholism at sea both among officers and lower-deck ratings is attributed to two main reasons—boredom and cheapness of spirits when available.

The duties of port health authorities are briefly stated and although food and sanitary services are said to be as good at sea as on land, therapeutic services compare very unfavourably with those on shore.

The method of recruitment of doctors for the Merchant Navy is criticized and it is stated that the quality of the average ship's surgeon is not high. The care of the sick in ships not carrying a surgeon [*i.e.*, a complement of less than 100] falls to the lot of the navigating officers or steward under the responsibility of the captain. The ship captain's medical guide is praised for its usefulness, but later in the article the author suggests that it should be revised more frequently as the current edition is more than 12 years old. [The current edition, however, was in fact revised in 1953 and brought up to date in 1957.]

Methods of recruitment by ship owners and the Shipping Federation are described and mention is made of the standards of fitness laid down by the Shipping Federation. Radiography of the chest is arranged for new entrants; the Shipping Federation is criticized for still making use of screening in this respect and for appointing examining medical officers with no special experience or knowledge of the sea as a condition of appointment.

With regard to the future, the author enlarges upon the mentality of seafarers as a whole and thinks that the ship owners are not fully aware that a sick or uninterested seaman is a bad investment.

The inoculation programme should be increased in scope and all sailors should receive regular immunization against typhoid and paratyphoid fever, BCG inoculation, Schick testing and protection against tetanus. Compulsory vaccination against poliomyelitis is advocated in addition to the existing requirements concerning quarantinable diseases.

There should be more study of the problems of survival and safety at sea; sailors should undergo more training to be conversant with the equipment in lifeboats. Maps and fishing tackle and modern apparatus for extracting salt from seawater should be available in all lifeboats.

Attention is drawn to the possible use of seaplanes, helicopters and hovercraft in saving life at sea and the suggestion is made that a hospital ship might be maintained at a strategic point on a trade route.

The introduction of nuclear energy for propulsion will necessitate new statutory regulations and the author is of the opinion that this will lead to the provision of better health services at sea with fewer but more highly trained personnel. *E. R. Peirce*

WORLD HEALTH ORGANIZATION. **Airports designated in Application of the International Sanitary Regulations. Situation as on 10 May 1960.** 18 pp. [In French & English.] 1960. Geneva. [fr.s. 1.–.; $0.30; 1s. 9d.]

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

MINISTRY OF LABOUR; CENTRAL OFFICE OF INFORMATION. **Health at Work. A Description of Medical Services in Fourteen British Factories.** 76 pp. 1960. London: Safety, Health & Welfare Dept., 19, St. James's Square, S.W.1.

"Experience in trying to encourage the development of industrial medical services suggests that a general statement of the aims and purposes and the arguments in favour of these services may well be accepted as generally true but lack the necessary impact to make an employer say: 'This might refer to me'." This introductory paragraph indicates why the Ministry of Labour with the help of the Industrial Health Advisory Committee has prepared this booklet. Its purpose is to provide practical information about the work of

medical services in industry, the reactions of the workpeople to them, and to show the actual advantages derived from these services which make the employers think it worthwhile to spend money and time on them.

Examples of 14 individual health schemes operating successfully in factories in different parts of Britain are given in some detail. The factories vary in size; 4 employ between 200 and 300 workers, 6 between 500 and 1,000 workers, the other 4 employing 1,149, 4,000, 5,540 and 8,000 respectively. The industries include heavy engineering and foundry work, steel making, copper and metal refining, the manufacture of electric cookers, refrigerators, electroplated ware, carbon block, printing machinery, animal feeding stuffs and vegetable oil. Also covered are wool and worsted spinning, the processing of asbestos yarns and pipes, and the preparation of insecticides, fungicides, fine chemicals and pharmaceuticals.

The details of each scheme are given at reasonable length under the same headings, namely health hazards, organization of medical services, accommodation and work of the staff, also details of ancillary services, where these are provided. Fear about costs having been suggested as the biggest single factor in preventing a more rapid spread of industrial health services, detailed particulars are given in the descriptions and include in every case the running costs covering salaries and medical supplies. In one instance (not described in the booklet) it was possible to set the cost of the scheme against the tangible savings, and the estimates are mentioned in the text. It is unfortunate that similar estimates were not made for the 14 schemes which have been described, but, this is always difficult to accomplish in industry.

No information is given on pioneer group schemes, which is a pity, for such schemes are the probable line of development in Britain in the foreseeable future. There are a significant number of factory estates with a sufficiency of factories and workers where modest group schemes employing a doctor and nurse could be started—and which could be self-supporting—*vide* the Poyle Estate Project of the Slough Industrial Health Service. Resistance from employers would be overcome and their collaboration obtained, provided some authority would take upon itself the function of active stimulation. In addition, it is likely that small and medium size factories in the older industrial areas will obtain a more effective industrial health service if they group together and employ experienced industrial nurses and medical officers, rather than depend on relatively infrequent and hasty visits from harassed general practitioners.

The booklet is clearly printed and the facts are succinctly given, but its style and presentation are sober and unimaginative, and one wonders whether the booklet will make any impact or create much interest in industry; particularly at the important level of top management. It is published on the assumption that there must still be considerable scope for the development of industrial health services on a voluntary basis. But is this so?, or has the time come when legislative pressure is required to promote an advance. The reviewer inclines to the latter view and, therefore, regards this booklet as a comparatively unimportant contribution to the progress of an increasingly important field of preventive medicine. *P. J. R. Challen*

JOHNSTONE, R. T. & MILLER, S. E. **Occupational Diseases and Industrial Medicine.**

This book was reviewed on p. 717.

PÉCHOUX, R. & KALB, J. C. L'examen physique et psychophysiologique des conducteurs de véhicules à moteur. [**The Physical and Psychophysiological Examination of Motor Drivers**] *Arch. Malad. Professionnelles.* Paris. 1961, Mar., v. 22, No. 3, 135–40.

Road safety presents many problems and among these is the human factor which is an important one in accident causation. In this paper the authors discuss the law in France which requires that all drivers of heavy vehicles and of public transport must submit to medical examination before a licence to drive is granted and also before a licence which has been withdrawn is granted anew. The conditions of this medical examination have been stated by decree and are here criticized.

In this paper there is an account of the findings in 3,000 drivers who have been examined in Lyons since 1954. Of these 43 were assessed as unfit to drive for a variety of physical or mental conditions which are stated. These disabilities are fully discussed with mention of the ways in which the certificates of unfitness to drive given after examination may be evaded or rendered inoperative.

Considerable emphasis is also placed on the importance of psycho-physiological examination which is practised in some centres in France but particularly in Lyons although it is as yet not a legal requirement.

M. E. Delafield

BERTOYE, A., HOUVER, A. & PERRIN, L. Quelques réflexions sur la pratique de la sélection et de la surveillance des machinistes de transport en commun urbain. [**Some Observations on the Selection and Supervision of Public Transport Workers**] *Arch. Malad. Professionnelles.* Paris. 1961, Mar., v. 22, No. 3, 141–3.

In this short paper the authors comment on their experience of the codified method of medical examination for the examination of transport drivers which was decreed by legislation in France in 1954. Attention is drawn to the shortcomings of this official method in respect of physique, vision, colour vision, and lack of precision, and also to the fact that illiteracy is not a bar to the acceptance of a candidate. Stress is also laid on the view of the authors that men who have any digestive troubles should be regarded as unsuitable.

Among other observations it is stated that about 23% of examinees were found to be unfit for the work. There are also some points on the diminishing frequency of accidents as the experience of the workers

increases with the years. Some figures on the incidence of lumbago and sciatica in these vehicle drivers are also given. *M. E. Delafield*

CHAYVIALLE, M. Expérience d'un Médecin du Travail chargé de la surveillance des chauffeurs de poids lourds et de transport en commun dans une usine de constructions automobiles. [**Some Experiences from the Medical Supervision of Heavy Transport Drivers**] *Arch. Malad. Professionnelles.* Paris. 1961, Mar., v. 22, No. 3, 143–5.

In this short paper there are recorded some observations on 90 chauffeurs made by the author during 10 years of his work as medical supervisor. The ages and years of work of these men are given with mention of their habits in respect of smoking and alcohol consumption, and the cardio-vascular, rheumatic and digestive troubles from which they had been found to suffer from time to time. Tuberculosis or a history of tuberculosis was found in 11 of the men. In the 10 years 9 chauffeurs died and 3 retired at 64 to 68 years of age.

Although the work of a chauffeur is arduous and complicated by difficulties and emergencies nevertheless it is stated that they love their work to which they remain loyal. It is also the opinion of the author that the medical disorders from which they suffer are no different from those experienced by workers in other occupations. *M. E. Delafield*

TILLMANN, R. Knochennekrose der Schultergelenke bei Tauchern. [**Bone Necrosis in the Shoulder Joint in Divers**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1961, Feb., v. 7, No. 2, 89–98, 9 figs.

Short references to some of the literature on bony changes in caisson workers and divers introduce this account of 2 cases of aseptic necrosis of bone in 2 divers.

There is a description of the work of these men at diving depths which in 1 of the men was at an average of 25 to 30 metres but sometimes as much as 55 metres. The incidents which led to attacks of " bends " are described.

Some clinical particulars are given and the appearances found on X-ray examination are to be seen in 9 photographs. The pathological changes were in the head of the humerus and consisted of necrosis of bone with evidence also of fracture and the formation of sequestra.

These cases were regarded as occupational in origin and hence subject to official notification and compensation. *M. E. Delafield*

HEINEN, W., FRIEDHOFF, E., MOHR, K., ZERLETT, G. & GÖRGES, T. Die Bedeutung der Mund-zu-Mund-Beatmung (Atemspende) für den Werksarzt. [**The Importance of Mouth-to-Mouth Artificial Respiration for the Factory Doctor**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1961, May, v. 11, No. 5, 105–9, 9 figs. [Numerous refs.]

OCCUPATIONAL PHYSIOLOGY

MACPHERSON, R. K. [Compiled by.] **Physiological Responses to Hot Environments. An Account of Work done in Singapore, 1948–1953, at the Royal Naval Tropical Research Unit with an Appendix on Preliminary Work done at the National Hospital for Nervous Diseases, London.** *Med. Res. Council Spec. Rep. Ser. No. 298.* pp. xv + 323, illustrated. 1960. London: H.M. Stationery Office. [35s.]

[This review appears also in *Trop. Dis. Bull.*, 1961, v. 58, 954.]

This report gives the results obtained during a 7-year programme of research carried out under the direction of the Royal Naval Personnel Research Committee of the Medical Research Council. The work was begun in 1944 at the National Hospital for Nervous Diseases in London, and was later continued at the Royal Naval Tropical Research Unit in Singapore.

In the London experiments the physiological effects of exposure to high air temperatures on men wearing different types of clothing were examined at different humidities and air speeds, both when the men were working and when they were resting. The subjects of these experiments had been artificially acclimatized by previous exposure to hot conditions in the laboratory, and on the basis of the results of the experiments tentative recommendations were made as to the conditions of warmth that were acceptable in ships at sea in tropical waters.

The results of these early experiments also seemed to show that the Effective Temperature Scale, which had been accepted for use as an index of warmth in HM Ships, was misleading in certain respects, and in consequence a new index, the Predicted Four-hour Sweat Rate (P4SR) was devised for the assessment of hot environments.

From the outset it has been recognized that investigations would have to be made in a tropical climate, and in 1948 the Royal Naval Tropical Research Unit was set up in Singapore. There, similar studies were made. These largely confirmed the earlier findings in London. Although they did not entirely support the criticisms of the Effective Temperature Scale, they did show that the P4SR was an accurate and convenient measure of the severity of indoor environments.

The work at Singapore was extended to compare the relative tolerance to heat of men who had been artificially " maximally acclimatized " in the laboratory and those who had been " naturally acclimatized " by residence in a tropical climate. The stress imposed by radiant heat of long wave-length and by different rates

of energy expenditure was also studied. Investigations to determine the upper limits of warmth that should be allowed in ships were extended to determine the upper limits that could be tolerated, and also the limits of the "comfort zone". Various other problems related to the main lines of research were also examined.

The main body of the report deals with the work carried out in Singapore, and an account of the work done earlier in London is given in an Appendix.

In the introductory chapter the wartime background and the later establishment of the Unit at Singapore are described. Then there are 8 chapters dealing with the various investigations, and at the head of each of these are given the names of those who took part.

The research was directed towards providing information which was required for specific purposes, and in the final chapter Dr. Macpherson discusses the extent to which those requirements were fulfilled. This chapter gives an admirable appraisal of the present state of knowledge on the assessment of environmental heat stress, the desirable upper limits of warmth, and the phenomenon of acclimatization. Concerning the first of these it is remarked that the assessment of the heat load imposed on man by solar radiation is one of the most urgent requirements of applied climatic physiology. Summing up the discussion on upper limits of warmth it is considered that "a knowledge of the physically tolerable levels of warmth is important, and equally so is a knowledge of the levels at which efficiency is likely to decline in the length of an ordinary working period; however it is more important to know, particularly for living quarters, the levels at which thermal comfort is experienced". Finally, it is concluded that the most important work yet to be done on the effects of hot environments on man is "the determination of the fundamental mechanism of acclimatization and the effect of exposure to heat over a period, not of hours or weeks, but of years, or even generations".

The arrangement of the report is excellent. The mass of detailed experimental results is given in a series of 123 tables following the main report, and in 17 tables following the Appendix. Thus all the pertinent statistical information is made available without interruption of the narrative.

This publication is an outstanding contribution to knowledge of climatic physiology. It will be of value not only to physiologists but to all who are concerned with life in hot climates or work in hot industries. All those who took part in this prolonged and exacting research are to be congratulated on the results achieved. Those who read the report will be grateful to Dr. Macpherson for the skill and patience that he has devoted to the arduous task of compilation, and for his clear review of the implications of the findings.

Thomas Bedford

CROCKFORD, G. W., HELLON, R. F., HUMPHREYS, P. W. & LIND, A. R. **An Air-Ventilated Suit for Wear in Very Hot Environments.** *Ergonomics.* London. 1961, Jan., v. 4, No. 1, 63–72, 6 figs.

In some situations in industry, or in the armed forces, work may have to be done in enclosed spaces where the temperature is very high, and where adequate cooling by ventilation is not practicable. In such circumstances some protection from the unduly hot environment is essential, and one convenient method of protection is the provision of a ventilated clothing assembly.

The authors describe experiments in which 15 men were exposed to an ambient temperature of 81°C. (178°F.) while wearing a ventilated suit assembly. The assembly comprised two special garments: (a) an undergarment made of a double layer of plastic film, the 2 layers being separated by a loose plastic filler; and (b) an outer garment of impermeable but pliable plastic material, with an attached cylindrical helmet made of a double layer of clear plastic with an intervening air space. The outer garment contained a 5 mm. layer of foamed plastic to act as an insulating barrier. The purpose of the undergarment was to distribute the ventilating air over a large area of skin.

The volume of air supplied to the suit ranged from 283 to 707 litres per minute (10–25 cu. ft. per minute), the temperature of the air was controlled to ±0·5°C. (0·9°F.) between 30° and 37·8°C. (86°–100°F.) as it entered the assembly, and the absolute humidity of the ventilating air was 6 to 7 mm.Hg.

At ventilating volumes of 424 litres per minute (15 cu.ft. per minute) and over the subjects were able to establish bodily thermal equilibrium in one hour irrespective of the temperature of the air supplied to the suit. When the supply was only 283 litres per minute (10 cu.ft. per minute) thermal equilibrium was never achieved.

In the interests of safety it is recommended that such a suit in use ought to be supplied with dry air at a volume of not less than 707 litres per minute (25 cu.ft. per minute) at a temperature of not more than 30°C. (86°F.).

Thomas Bedford

OCCUPATIONAL DISEASES

HIGGINS, I. T. T. & COCHRANE, A. L. **Chronic Respiratory Disease in a Random Sample of Men and Women in the Rhondda Fach in 1958.** *Brit. J. Indust. Med.* 1961, Apr., v. 18, No. 2, 93–102. [23 refs.]

Mortality and morbidity rates show that South Wales coal-miners are unduly prone to bronchitis [HIGGINS *et al.*, this *Bulletin*, 1956, v. 31, 1233; 1957, v. 32, 50; 1959, v. 34, 238; 1960, v. 35, 964]. In order to throw some light on the respiratory disability of miners in the Rhondda Fach, the authors have made a survey of respiratory symptoms and ventilatory capacity of a random sample of 600 men aged 35 to 64 years of age, and of 200 women between 55 and 64 years of age. Respiratory symptoms were recorded by a

questionnaire, the ventilatory capacity by measuring the 0·75 second forced expiratory volume (FEV). A postero-anterior chest radiograph was also taken. The samples were stratified in age and occupation; 100 ex-miners and miners, and 100 non-miners in each decade.

The results found were that miners with simple pneumoconiosis did not have lower values for ventilatory capacity than those without pneumoconiosis at any age. Miners with progressive massive fibrosis (PMF) showed a significant reduction at all ages. Symptoms were increased in miners who had been over a year underground but there was no consistent increase with longer duration. There was an overall downward trend in the mean indirect maximum breathing capacity (MBC) with time engaged on coal getting: this trend however did not reach the 5% level of statistical significance. It appeared in miners without pneumoconiosis and in those with PMF. It did not appear in those with simple pneumoconiosis: simple pneumoconiosis however may progress to PMF. Analysis of the figures for lung function of miners and ex-miners separately suggested that at age 55–64 the decline was greater in the working miner. Analysis of the findings in women showed that miners' wives recorded a higher prevalence of symptoms and a lower indirect MBC than non-miners' wives.

The authors discuss the causes of these occupational differences in respiratory affections between miners and non-miners. General atmospheric pollution does not play a part. Tobacco consumption could not account for the differences between miners and non-miners since these remained after standardization for smoking. Genetic differences involving increased susceptibility are unlikely to affect only the miners. Social class differences as shown by the results in the 200 women are important. As regards dust, it is difficult to show any close relation between dust exposure and either symptoms or lung function in miners and ex-miners in the area. It might have been expected that miners with simple pneumoconiosis would have been more affected with bronchitis and disability than miners without such radiological change but there is little difference between them. The age of entry into underground work may be a factor in causing the regional difference in respiratory disease in South Wales.

Charles L. Sutherland

World Health Organization. Technical Report Ser. No. 213. **Chronic Cor Pulmonale. Report of an Expert Committee. Geneva, 10–15 October, 1960.** 35 pp. 1961. Geneva: Palais des Nations. [Sales Agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

This is a report on chronic cor pulmonale by the WHO Expert Committee which included authorities from many countries. Professor D. W. Richards of New York was in the chair and Professor C. H. Stuart-Harris was rapporteur.

The objectives of the report were: (i) to define chronic cor pulmonale in terms useful for further discussion; (ii) to provide a tentative classification of diseases which may be the cause of this syndrome; (iii) to describe in broad terms the pathophysiology of cor pulmonale and to establish criteria for diagnosis.

Cor pulmonale is defined as "Hypertrophy of the right ventricle resulting from diseases affecting the function and/or the structure of the lung, except when these pulmonary alterations are the result of diseases that primarily affect the left side of the heart or of congenital heart disease." Diseases which may be the cause of cor pulmonale were classified broadly as: (i) Diseases that primarily affect the ventilatory and respiratory function of the lungs. (ii) Diseases that act directly on the pulmonary vessels. Detailed tables of causes are given under these headings.

If mortality statistics are to provide information on chronic cor pulmonale provision should be made for indicating its aetiology in the next revision of the detailed list of the *International Classification of Diseases*, and one suggestion is that a new three-digit title should be provided for cor pulmonale with a fourth-digit sub-division under this title according to aetiology. A suggested list is given in a table. Another possibility is to provide two fourth-digit sub-divisions "with pulmonary heart disease" and "without pulmonary heart disease" under those existing aetiological categories which are of sufficient importance to warrant such sub-division. The latter proposal is favoured since it would conform better with present practice of codification.

The major part of the report is concerned with physiological derangements, clinical recognition, treatment and prevention. A final section is devoted to suggestions for research and recommendations, which are epitomized in the final paragraph:

"The Committee believes that WHO as an international organization with world health as its concern is particularly well placed:

"(a) to encourage, sponsor and co-ordinate those aspects of research for which an international approach is needed, e.g. field surveys where comparative studies in different parts of the world are essential;

"(b) to promote the use of comparable nomenclature, classification and diagnostic criteria and methodology in general;

"(c) to convene meetings of an international nature;

"(d) to encourage training in research requirements."

This report should be read in full. It cannot be adequately summarized since it is itself a succinct account of world opinion on all aspects of the subject.

G. F. Keatinge

Broomhead, G., Hodkinson, J. R. & Simons, V. **Photometric Evaluation of Konimeter and other Dust Samples.** *Safety in Mines Research Establishment.* [Portobello St., Sheffield, 1.] *Research Rept.* No. 191. 1960, Aug., 19 mimeographed pp., 4 figs. [38 refs.] [2s.] [Translated from *Staub*, 1960, May 1, v. 20, No. 5, 144–50.]

Some earlier measurements are discussed of the reduction in intensity of a light beam, or extinction, when passed through a sample of dust on the glass plate of a konimeter. The light cone, leaving the specimen of dust, had a semi-angle of about 20° and

most of this light fell upon the photoelectric cell used for measuring intensity. Such measurements are termed wide-angle extinction measurements.

The absorption of light in opaque particles contributes to the extinction but when measured over a wide angle some of the light deflected or scattered by the particles is permitted to reach the photocell and a lower extinction is recorded. If all the scattered light from opaque particles is accepted their extinction is proportional to their total area normal to the light beam, for particles sampled by the konimeter, as was shown in one series of experiments described. Hence, for a constant size distribution, a linear relationship is observed between light extinction and number of particles.

In another series of experiments, instead of straight lines, curves concave towards the extinction axis resulted. This was caused by visual counting being more susceptible to the overlap of particles at high sample densities than light extinction.

The wide-angle extinction of deposits of transparent particles will be lower than that of equivalent opaque ones but differences in opacity can be eliminated by measuring extinction with a narrow angle of acceptance of scattered light. Such measurements can only be made with specially designed optical systems and it is important that the medium carrying the dust particles should not scatter light. Samples of dust on filter paper, for example, effectively scatter over a wide angle under all circumstances and show the extinction of opaque dust alone. Narrow angle measurements are complicated by rapid variation of the light extinction with particle size which passes through a maximum in the neighbourhood of half a micron diameter. The extinction is also sensitive to the angle of acceptance.

Measurement of light scattered at a given angle from the direction of the original beam, in contrast to extinction measurements with wide or narrow angles of acceptance, has long been used in the Tyndalloscope which operates at 30°. More light is available from transparent particles than from opaque ones, limestone dust giving nearly 4 times as much as coal for dusts of equal projected area. This difference is mainly due to light which enters the particles and is reflected by them. Apart from variation in transparency, angular scattering at 30° appears to be proportional to the surface area of dust and insensitive to its refractive index.

Combination of narrow angle extinction (independent of transparency) and angular scattering at about 30° (much greater for transparent particles) might enable the proportion of black and transparent components in a mixed dust to be determined. *C. N. Davies*

HOSEY, A. D., JONES, H. H. & AYER, H. E. **Evaluation of an Aerosol Photometer for Dust Counting and Sizing.** *Amer. Indust. Hyg. Ass. J.* 1960, Dec., v. 21, No. 6, 491–501, 8 figs. [14 refs.]

The instrument, which weighs 10½ lbs., is entirely contained in a case measuring 5″ × 8½″ × 15″; rechargeable batteries and mercury cells are used. Aerosol is admitted through a dilution valve controlling the concentration between 1:1 and 1:20 which enables full-scale deflections between 5 million and 100 million particles per cu.ft. to be read. Sampling is effected by a governor-controlled gear pump at 17 cm³ per minute which is checked periodically by the soap film method. Light pulses scattered by individual particles as they cross the focus of a light beam are received by a photocell and amplifier and fed into an amplitude discriminator, where an output voltage is produced which is proportional to the number of pulses per second. The discriminator circuit can be adjusted manually in steps of 0·1 micron to count only particles larger than a preselected size in the range of 0·3 to 2 microns. Larger sizes are counted but not sized. The instrument is calibrated with an aerosol of Dow polystyrene latex spheres.

Test dusts were dispersed in the laboratory and the aerosol photometer was compared with the standard impinger dust counting technique; ratios obtained varied with the dust and could be adjusted to agree within ± 15% by an appropriate setting of the discriminator of the photometer. Size distributions obtained with the photometer suggested that it records particles which are too small to be visible by oil immersion microscopy; on the other hand, it appears to miss large particles. *C. N. Davies*

DAUTREBANDE, L., DECKMANN, H. & WALKENHORST, W. Licht- und elektronenmikroskopische Untersuchungen zur Abscheidung von Staub in den Atemwegen. [**Measurements of the Deposition of Dust in the Respiratory Tract by Visual and Electron Microscopy**] *Staub.* Düsseldorf. 1961, Mar. 1, v. 21, No. 3, 141–51, 15 figs. [32 refs.]

Various theoretical and experimental estimates, collected by Hultqvist, of the total deposition of particles in the lungs during breathing, and of deposition in the deep lung, or alveolar regions, are reproduced. Only the former is directly measurable.

An apparatus for measuring total deposition is described. The subject inhales dust from a chamber through a mask provided with inlet and outlet valves. Both inhaled and exhaled air are sampled with thermal precipitators and the size distributions determined by visual and electron microscopy. The dusts ranged from Indian ink and titanium dioxide, having a mean particle diameter of 0·09 micron, to coal dust of 0·75 micron. Inhalation in all cases was through the nose. Frequency of respiration was controlled by a stopwatch or by breathing in time with a metronome at 3, 10 and 32 cycles per minute; the average volumes inhaled per breath were 2,100, 810 and 380 cm³ respectively.

As well as sampling the dust in exhaled air, after mixing so as to obtain an average over the duration of expiration, arrangements were made to secure samples of the air at the end of a normal breath and of the Haldane-Priestley alveolar air at the end of a strong forced exhalation following the conclusion of a normal breath. Particles found in these terminal samples would come from the alveoli without deposition while ascending the bronchioles and bronchi.

The experiments showed that deposition, expressed as a percentage of the amount of dust inhaled, was much higher in the Haldane-Priestley air than in the air at the end of a normal exhalation for which the figure exceeded, in turn, the total average deposition. At respiration frequencies below 32 cycles per min. deposition in total air and at the end of a normal respiration increased but no change with frequency was found for alveolar air.

Minimal deposition in the total air occurred between 0·25 and 0·6 micron diameter and did not vary much with frequency of breathing. The minima were near to 0·5 micron for coal dust and between 0·2 to 0·3 micron for others. The deposition-particle size curve for total air, with coal dust, agrees well with previous experiments by LANDAHL *et al.* [this *Bulletin*, 1951, v. 26, 906] using a mist of triphenyl phosphate. Some indication of minimal retention in the alveolar air was obtained at 0·15–0·25 micron with Indian ink and calcium carbonate.

Some experiments in which the subject inhaled oxygen-enriched air and then held his breath for up to 35 seconds demonstrated deposition from alveolar air increasing with the duration of breath-holding.

The size distributions of inhaled dust and the dust in total, end of respiration and alveolar air are almost identical when a fine dust, with all particles below 0·7 micron, is inhaled. With a coarser dust, however, there is a progressive and marked disappearance of larger particles. *C. N. Davies*

NANN, A. Untersuchungsergebnisse über die Quarzstaubgefährdung einer Steinbruchbelegschaft. [**Results of an Investigation into the Quartz-Dust Hazard to Workers in a Quarry**] 39 pp. [12 refs.] 1959. Zürich: Zürcherische Arbeitsgemeinschaft zur Erforschung und Bekämpfung der Silikose in der Schweiz.

This paper has been presented as a doctorate thesis to the University of Zurich. It gives an account of the legal provisions for compensating sufferers from silicosis. The regulations in force at present are contained in the Federal Council's Order of September 3rd 1948 which covers all workings where materials with more than 10% quartz are used or worked.

The main part of the paper is devoted to a study of the silicosis found at a particular quarry where the stone has a silica content of 45 to 70%. The stone-dressers and masons work in a shed divided into compartments for each worker. These working places are open at each end. Hammer and chisel are the tools used. The stone-splitters use compressed air hammers to punch the holes for the iron wedges. The miners use compressed air drills in the process of blasting to excavate the usable rock. Miners may be employed part time as splitters. The navvies have a risk in that they move the stone from the splitters to the masons and dressers.

53 patients with silicosis were investigated. They were grouped into (1) those exposed only in the working. (23); (2) those chiefly exposed in the working. (16); (3) those chiefly exposed in another working (14). The results reported showed that no constitutional type could be recognized as specially liable. Two-thirds of the patients were Italians, a proportion corresponding to the composition of those employed in the working. Mouth breathers were more liable. The average period of exposure of each of the groups was 16·8, 18·7, and 20·8 years, respectively. The period of exposure varied very considerably both in those whose work was continuous and those whose work was interrupted. The first group contained the greatest number of early cases whose condition could only be detected by X-ray. Such patients did not qualify for pension. No evidence as to the effect of early age of entry into the work could be obtained. 2 cases of open tuberculosis were found in each group. In group 1 and group 3 half the patients were off work for shorter or longer periods owing to lung complaints; in group 2 rather more than one-third.

Prophylaxis from the medical angle consists of an examination on entry to exclude unsuitable workers, that is those with possible tuberculosis and those with obstructed breathing. Periodical examinations will allow men with incipient silicosis to change their jobs.

Technical prophylaxis by means of extraction plants is difficult and expensive. Wetting the stone is not successful because of the compact nature of the stone. Fresh-air masks are to be preferred since they offer no obstruction to breathing and need not be tightly fitted to the head.

[An outstanding omission in this investigation is the absence of physiological lung function tests.]

Charles L. Sutherland

VIGLIANI, E. C. Quelques considérations sur la théorie immunitaire de la silicose. [**The Immunity Theory of Silicosis**] *Med. d Lavoro.* 1960, Nov., v. 51, No. 11, 655–9, 2 figs.

The author's views on the pathogenesis of silicosis have altered with the progress of knowledge of immunity and of the functions of the reticulo-endothelial system. His papers published before 1957 may give rise to wrong conclusions. He therefore indicates in this paper the lines on which he is now pursuing his investigations. He recapitulates the facts:—

(1) Free crystalline silica is toxic only to the cells, the macrophages, which ingest the particles. The cells are killed, one after the other, slowly perhaps over a period of years.

(2) After the death of the macrophages has commenced, the following events occur:— (a) Numerous fibrocytes appear and form a reticulum of collagenous fibres. (b) Plasmocytes congregate round the collection of macrophages and in the tributary lymphatic nodes. (c) Gamma globulins are precipitated on the collagenous fibres of the silicotic granuloma. (d) There is an increase in the production of antibodies against antigens without relation to the quartz. (e) There are variations of the phagocytic activity of the RES, of resistance to infections by Gram-negative organisms, and of the susceptibility to the toxic action of endotoxins. (f) Certain antibodies of feeble specificity, such as zymosan-agglutinins and the rheumatoid factor, appear or are augmented in the serum.

Of all the phenomena associated with the death of the macrophages, the most interesting from the immunological point of view are the appearance of plasmocytes and the precipitation of gamma globulins on the collagenous fibres. The author believes that these indicate the production of antibodies.

There are two immunity theories of silicosis. The theory of specific immunity advanced by SCHEEL in America, by ANTWEILER, and by ISHINISHI and other Japanese workers, is that crystalline silica adsorbs proteins and denatures them to as to render them auto-antigenetic. The second theory (PERNIS and VIGLIANI) postulates non-specific immunity. According to this theory quartz is not antigenic, or capable of transforming proteins into auto-antigens. Quartz is simply an immunological adjuvant capable like all adjuvants of activating the RES, and of increasing antibodies *vis-à-vis* all antigens. This theory is now held by ANTWEILER. This adjuvant action only appears when the macrophages begin to be killed by the quartz.

The author sets out the various questions which have yet to be answered before the pathogenesis of silicosis is explained. This work demands the collaboration of industrial doctors with immunologists, biochemists, biophysicians and requires considerable financial means.

Charles L. Sutherland

STRUKOV, A. I. & RAIKHLIN, N. T. **Connective Tissue in Experimental Silicosis and Anthracosis. Histochemical Features of Development.** *Arch. Pathology.* 1961, Feb., v. 71, No. 2, 142–50, 8 figs. [29 refs.]

The present paper is concerned with a comparative study in experimental silicosis and anthracosis. 122 white rats were used in 3 series of experiments. In the first, experimental silicosis was induced in 76 rats by the intratracheal introduction of 50 mgm. silicon dioxide in sterile saline; in the second, 35 rats were given 50 mgm. coal dust containing 0·5% silicon dioxide in sterile saline solution; in the third, 11 rats which were given saline solution alone served as controls.

In experimental silicosis the development of connective tissue begins with the appearance of non-differentiated fibroblasts, rich in ribonucleic acid, which are rapidly transformed into fibrocytes. Sections from silicotic lungs treated with collagenase solution for 48 hours became stain-resistant to picrofuchsin, but fibres from normal lungs did not behave in this fashion. In experimental anthracosis, on the other hand, sections treated with collagenase for 48 hours retained their staining reaction to picrofuchsin.

Recent literature concerning the nature of collagen is reviewed, and special reference is made to TUSTANOVSKY and his colleagues (*Problems Med. Chem.*, Moscow, 1951, v. 3, 176; *Rep. Acad. Sci.*, U.S.S.R., 1954, v. 97, 121), who divided collagen into two phases, soluble procollagen and insoluble collastromin, and to another paper dealing with the action of toxin-collagenase —from *Clostridium welchii* (Type A)—in which it was shown that only procollagen of all the connective tissue proteins is capable of being split by this substance. It is held that procollagen is bound quite loosely with the rest of the fibre collastromin, and the authors are in agreement with the concept of MICHAELIS and GRANICK (*J. Amer. Chem. Soc.*, 1945, v. 67, 1212) and of others that the character of the metachromasia depends upon the degree of polymerization of the mucopolysaccharides.

In silicious connective tissue, formation of incomplete collagenous fibres occurs, and as a result the fibres undergo considerable adjustment, and become disarranged. Accumulation of products of the collagen complex in the tissue and their subsequent combination are conducive to the appearance of hyalinosis. Necrosis of silicious nodules is closely connected with poorly formed collagen fibres.

Mention is made of the work of CHVAPIL (*Physiol. Bohemoslovenica*, 1956, v. 5, 421), who showed that in silicosis, in the lung tissue, there is an increase in hydroxy-proline-containing proteins much earlier than in the fibrous tissue, and SMITH and JACKSON (*Biochem. J.*, 1956, v. 64, 8p) demonstrated the formation by fibroblasts of ^{14}C hydroxyproline from ^{14}C proline. In the light of this work, the theory of HOLT and OSBORN [this *Bulletin*, 1953, v. 28, 830] that silicic acid may act as a filling material in the collagen network is an over-simplification.

During experimental anthracosis the development of sclerosis proceeds at a slow rate and never reaches the degree attained in silicosis. The manifestations of hyalinosis are less pronounced while necrosis of the fibrous dust foci is rare. Of major importance in the mechanism of the collagenous fibre production, is the acellular type of sclerosis.

[This paper is somewhat diffuse and the argument at times hard to follow, which may be due to the English which is far from simple.] *G. F. Keatinge*

HEPPLESTON, A. G., AHLQUIST, K. A. & WILLIAMS, D. **Observations on the Pathogenesis of Silicosis by means of the Diffusion Chamber Technique.** *Brit. J. Indust. Med.* 1961, Apr., v. 18, No. 2, 143–7. [25 refs.]

Experiments with the diffusion chamber technique were made to test the validity of the solubility theory of silicosis. The technique was modified from that of ALGIRE *et al.* (*J. Nat. Cancer Inst.*, 1954, v. 15, 493). The dusts tested were (a) 4 physical forms of silica, tridymite, crisobalite, quartz, and vitreous silica, (b) Aerosil, a silica gel and (c) anthracite. The chambers were placed in the flanks and peritoneum of rats and rabbits. Control chambers were also employed. The result found was that reaction round the dust chambers was either similar to or less than that shown by controls and was uninfluenced by the type of dust used. These results agree with those of PERNIS *et al.* [this *Bulletin*, 1959, v. 34, 454] and of CURRAN and ROWSELL [*ibid.*, 452]. It is suggested that polymerized (colloidal) silicic acid, the form which is toxic and may be fibrogenic, does not escape from the chambers. CHVAPIL and HOLECKOVÁ [*ibid.*, 1961, v. 36, 121] found in their experiments that there was a level of silicic acid concentration above which the fibrogenic effect was inhibited, and a lower concentration which had no

effect. KNAKE *et al.* [*ibid.*, 1960, v. 35, 542] found that weak (monomeric or oligomeric) silicic acid had no effect on cultures of rabbit spleen and lung.

Below a critical concentration silicic acid exists as low polymers or monomer, whereas above this level the acid consists of higher polymers. It may be argued that polymerized silicic acid only is concerned in fibrosis. The authors do not believe that this type of experiment can be used to decide the validity of the silica solubility theory. Closer contact is needed between cells and silica than the membranes permit.

Charles L. Sutherland

ENGELBRECHT, F. M. & BURGER, F. J. Die invloed van kolloïdale silika op die suurstof-verbruik van weefsels. **[The Influence of Colloidal Silica on the Oxygen Uptake of Tissues]** *South African J. Lab. & Clin. Med.* 1960, Dec., v. 6, No. 4, 217–25, 1 fig. [17 refs.]

In an address given at the University of Stellenbosch, South Africa, the authors describe various theories of the aetiology and pathogenesis of silicosis and their own investigations.

In view of the findings of MARKS and his associates [this *Bulletin*, 1957, v. 32, 47], the authors investigated the influence of various forms of silica on the oxygen uptake in rat liver, lung, spleen, kidney and heart *in vitro*. SÖRENSEN and KREBS Ringer-phosphate buffers were used as media. Colloidal silica was used in accordance with the method of HOLT and BOWCOTT [*ibid.*, 1954, v. 29, 1160]. The oxygen uptake was measured in a Warburg apparatus over a period of 6 hours.

The change in the oxygen uptake in liver, spleen, kidney and lung tissues in the presence of colloidal silica was found to be not statistically significant. The authors suggest that the failure of colloidal silica substantially to affect oxygen uptake of the tissues might have been due to the impermeability of the cell membrane to the large molecules of colloidal silica, so instead monomeric silica was added and allowed to polymerize over a period of 16 hours. Krebs Ringer-phosphate buffer was used as medium. The inhibition of oxygen uptake was over 50% in all experiments, and as much as 75% in some. It thus appears that colloidal silica is not the important aetiological factor it was thought to be, and that monosilicic acid is the more likely cause of silicosis. This substance in itself is harmless, but it can penetrate the cell membrane and then polymerize to form colloidal silica, which would then be the aetiological agent.

Anne Tothill

SCHLIPKÖTER, H. W. & LINDNER, E. Elektronenmikroskopische Untersuchung von Quarzgranulomen bei der experimentellen Silikose der weissen Ratte. **[Investigation by the Electron Microscope of Quartz Granulomata in Experimental Silicosis of White Rats]** *Ztschr. f. Hyg. u. Infektionskr.* 1961, v. 147, No. 3, 287–318, 23 figs. [26 refs.]

The investigation of the histology of silicosis is made difficult by the hardness of the crystal and by its size (under 3 μ) in comparison with the extremely thin section required (40–80 mμ). The authors have got over this difficulty in their study of the lungs of white rats. The rats were given intratracheal injections of a specially prepared quartz flour suspended in distilled water. They were then killed at intervals of 6 months and 1 year.

23 illustrations of the histology of these lungs under the electron microscope are presented and the changes are carefully demonstrated. In the discussion the process of phagocytosis of the particles and the results are described. The dust particles pass into an invagination of the cell membrane which closes behind them, so that they come to lie enclosed in a membrane inside the cell. The jagged quartz crystals, however, are found lying free in the cytoplasm and it is presumed that their sharp edges cut the membrane. Among reasons given for this supposition is the observation of POLICARD *et al.* that amorphous silica dust retains the membrane after phagocytosis. Other hard substances such as corundum and carborundum may also cut the membrane but their chemical and minerological characters do not lead to fibrosis.

The investigation shows that in silicotic granuloma there is much damage to the mitochondria. The cells themselves break up and form "ruin zones". The connexion of this cell destruction with the immunological theory of silicosis is mentioned. The products of the destruction of cells pass between the fibrils of collagen. The destruction of the basal membrane observed by Policard, as a result of the reaction to amorphous silica, was also found in these lungs.

Charles L. Sutherland

CARTOUZOU, G., DEPIEDS, R., LISSITZKY, S. & DUPLAY, J. Étude électrophorétique de certains constituants protéiques solubles du granulome silicotique péritonéal expérimental. **[Electrophoretic Studies of Certain Soluble Protein Constituents of Experimental Peritoneal Silicotic Granulomata]** *C.R. Soc. Biol.* 1960, v. 154, Nos. 8/9, 1560–67, 7 figs. [10 refs.]

The silicotic granulomata induced in rats and guinea-pigs by the intraperitoneal injection of 3 μ or 20 μ silica particles, contain proteins which are partly (5–20%) fibrous, related to collagen, and partly non-fibrous. The proteins have been fractionated into non-collagenous proteins (I and II) alkali-soluble collagen (III), acid-soluble collagen (IV), insoluble collagen transformed into soluble gelatin (V), non-collagenous fraction soluble in 0·1 N NaOH (VI) and an insoluble residue (VII). Fractions I and V were subjected to paper electrophoresis at *p*H 8·6 and *p*H 6·2.

Fraction I from the rat, at *p*H 8·6 showed a fast-moving band in the serum albumin region and a slow-moving band in the region of the beta globulins. At *p*H 6·2 a fast-moving constituent appeared in the region of the alpha globulins and a slow-moving constituent with the gamma globulins. Fraction I from the guineapig, *p*H 8·6, had one constituent which moved with the albumins and a major constituent with the alpha globulins. At *p*H 6·2 a band moved behind the gamma globulin.

Fraction V from the rat, at *p*H 8·6, gave a band in the region of the beta globulins, similar to that given by

pure gelatin and at *p*H 6·2 a band similar to that of the beta-gamma globulins. Fraction V from the guinea-pig gave two bands in each case. *P. F. Holt*

SAITA, G. & GALLI, T. L'attività antitrombinica plasmatica nella silicosi. [**Plasma Antithrombin Activity in Silicosis**] *Med. d. Lavoro.* 1961, Jan., v. 52, No. 1, 14–28. [Numerous refs.] English summary.

Modern views on the physiological role of antithrombin are discussed and the immunological theory propounded by VIGLIANI and his colleagues [this *Bulletin*, 1961, v. 36, 1] as a cause of silicosis suggests that in certain respects it has a relationship with the so-called collagen diseases.

"Anticoagulent substances having antithrombin activity may appear in the plasma in disorders with an immunological basis, such as collagen and autoimmune diseases; these anticoagulants sometimes show heparin-like antithrombin activity, but sometimes they are not neutralized by protamine and have other unusual characteristics. The presence of these anticoagulant substances has been related to the altered plasma protein pattern, and some workers believe them to be non-specific antibodies. On the basis of the above data, the authors have investigated antithrombin activity in 34 cases of silicosis, by means of prothrombin time determinations; the prothrombin time was found to be raised in 9 cases of advanced silicosis which showed dysproteinaemia and non-specific serum immunological factors; these were often associated with active or latent tuberculosis. The prothrombin time was never found to be raised in cases of early silicosis showing no dysproteinaemia. The anticoagulant appeared to have properties similar to those of heparin; it was present in plasma, but little in serum, it was regularly neutralized by protamine; it disappeared on heating the plasma to 56°C; it was partially absorbed by barium sulphate but not by calcium carbonate or by aluminium hydroxide; *i.e.*, it appeared to have the properties of a heparin-like anticoagulant. The biochemical characteristics of this anticoagulant are not those of an antibody. The raised level of antithrombin activity found in silicotics is probably dependent on the liberation of heparin, secondary to the proliferation and degranulation of mast cells in the silicotic nodules. Hepatic lesions, due to toxaemia, tuberculosis or circulatory stasis, may play an additional part in increasing antithrombin activity."

G. F. Keatinge

HERVAN, M. S. A propos de deux cas de silicose retardée. [**Two Cases of Delayed Silicosis**] *Arch. Malad. Professionnelles.* Paris. 1961, Mar., v. 22, No. 3, 164–5.

SCHEPERS, G. W. H. & DELAHANT, A. B. **Prevention of "Silica Shock" by Aluminum. An Experimental Exploration on Guinea Pigs of the Antidotal Properties of Four Varieties of Aluminum.** *Arch. Environment. Health.* Chicago. 1961, Jan., v. 2, No. 1, 9–15, 6 figs. [12 refs.]

The authors cite evidence that the physiological manifestations of quartz exposure originate in smooth muscle spasm, and state that any prophylactic or therapeutic agent must be assessed with reference to its ability to counteract this action as well as to suppress granuloma formation and fibrosis.

GARDNER (*Experimental Pneumoconioses, Silicosis and Asbestosis*, Ed. A. J. Lanza, New York, 1938, O.U.P.) had noted that rabbits receiving 0·1 gm. of particulate silica in a single dose intravenously promptly developed acute symptoms of shock and died. At necropsy the dominant finding was intense engorgement of the splanchnic vessels. The present report records the results of the use of this "silica shock" phenomen in the study of the antidotal properties of 4 aluminium agents to silica. Guineapigs were used and it was found that 4 cc. of 1% quartz (40 mgm. SiO_2) injected intracardially were effective in producing "silica shock." The agents used were colloidal aluminium hydroxide, $Al(OH)_3$, precipitated aluminium hydrate H_{1010}, oxidized metallic aluminium M38, and metallic aluminium DR, the sources of which are given.

It was found that "silica shock" was absolutely prevented by adding 4 to 26 mgm. of colloidal aluminium hydroxide to the suspension, but the other 3 agents were inadequate antidotes and, in the case of precipitated aluminium hydrate, even intensified the splanchnic vascular reaction. Reference is made to previous work [DWORSKI, this *Bulletin*, 1956, v. 31, 37; GARDNER, *et al.*, *ibid.*, 1945, v. 20, 204], which showed that in guinea-pigs, hepatic and splenic silicotic cirrhosis may be prevented by simultaneous injection of colloidal aluminium hydroxide, or lessened by administration as late as 6 months after the introduction of the silica. Colloidal aluminium hydroxide is non-toxic on intracardial injection within a therapeutically effective dose-range and it is suggested that, given intravenously it may mitigate disabling bronchiolar spasm and pulmonary hypertension in silicotic patients. *A. T. Doig*

REUSCH, G. Kasuistischer Beitrag zum Problem der Aluminiumlunge. [**A Contribution to the Problem of Aluminium Pneumoconiosis (Case—Report)**] *Deut. med. Woch.* 1961, Mar. 24, v. 86, No. 12, 520, 525–8, 533, 9 figs. on 2 pls. [29 refs.]

This is a review of the present ideas on aluminium lung, in which various authorities are quoted. The diagnosis of aluminium lung is based on radiological investigation, on spirometric tests of lung function, and by demonstration of aluminium in the sputum. Aluminium can be shown by embedding the sputum in paraffin and staining with morin, a vegetable dye. Aluminium-containing portions of tissue in the sputum are shown by their light yellow colour. The case described is that of a man of 27 years of age who was still spitting up aluminium-containing sputum 2 years after the end of his exposure. He had been smelting aluminium for 6 years. The radiograph of the chest showed enlarged roots, increased striation of the lung fields with collections of small opacities interspersed in the lung. The results of the spirometric tests are detailed: the lung function was limited. JÄGER and JÄGER [this *Bulletin*, 1943, v. 18, 394] are quoted as believing that the aluminium-containing pieces of lung tissue brought up with the sputum result from a

destructive process. Even after cessation of exposure, more aluminium is dissolved. Everything should be avoided which will accelerate the appearance of aluminium ions. Mercury has this action and Jäger warns against dental repair with mercury amalgam. From this viewpoint, the disease results from a chemical and not from a mechanical effect: the correct name therefore should be aluminium lung and not aluminium dust lung.

The production of stearin is still deficient in peacetime so that there is only a qualitative difference between the rapidly progressive wartime disease and the more slowly progressive peacetime type.

The difference between aluminium lung and silicosis lies in the discrepancy between the severity of the disease and the short duration of exposure in the former. In younger people the progress is rapid and frequently spontaneous pneumothorax occurs. Severe aluminium lung presents an unsuitable medium for the development of tuberculosis, but lesser changes do not protect from tuberculosis. The experiment of aluminium prophylaxis in animals gave positive results but its prophylactic action in man has yet to be established.

Charles L. Sutherland

ABDEL-SALAM, M. S. **Dust Exposures in Egyptian Foundries.** *Ann. Occup. Hyg.* London. 1961, Feb., v. 3, No. 2, 107–13, 1 fig.

Following a survey in 1958 of one foundry [VALIC *et al.*, this *Bulletin*, 1960, v. 35, 967 *bis*], 9 other foundries were surveyed. None with less than 10 employees were included although these constitute over 50% of Egyptian foundries. In each foundry, all operations take place in the same hall: in 2 this comprised merely a roof with no walls. No means of dust suppression were employed except in 2 of the foundries where wetting of clay and sand is undertaken.

Tables show the quartz content of the dust in various locations (12·5 to 72%), and the maximum, minimum, and mean dust counts at different operations in individual foundries. Dust levels were high, though lower than in the earlier investigation. The general dustiness exceeded the recommended MAC in 5 of the 9 foundries. Screening of dry materials was especially bad (mean 279 million particles per cu. ft.). Wetting before screening led to a striking reduction of dust. Individual operations are not described. The use of water is advocated and the recommendations suggested by Valic *et al.* are summarized.

A. T. Doig

SHAPTINI, E. A. **Byssinosis—a Review.** *Indust. Med. & Surgery.* Miami. 1961, Mar., v. 30, No. 3, 95–100. [13 refs.]

CAVAGNA, G. & FINULLI, M. Attività istaminoliberatrice nel sottocutaneo di ratto di endotossine contenute nel cotone. [**The Histamine Liberating Power of Cotton Endotoxins studied on Rat Subcutaneous Tissue**] *Med. d. Lavoro.* 1961, Jan., v. 52, No. 1, 43–6. [14 refs.] English summary (9 lines).

Byssinosis has been variously attributed to the effect of bacteria, fungi and to allergens present in cotton. Recent work by PERNIS *et al.* (*Brit. J. Indust. Med.*, 1961, v. 18, 120), has demonstrated the presence of endotoxins of Gram-negative organisms in cotton dust and it is thought probable that they may be included among the substances present in cotton which are responsible for the liberation of histamine.

This paper describes some investigations undertaken by the authors which lend support to the view that endotoxins are not the only substances in cotton dust which are capable of causing the liberation of histamine. The histamine-liberating power of endotoxins contained in cotton was studied by using subcutaneous tissue from a rat's leg.

"The following have been used: an aqueous cotton extract, an extract in a water-phenol medium (method used by WESTPHAL *et al.* (*Ztsch f. Naturforsch.*, 1952, v. 76, 148) for the isolation of endotoxins), and finally purified endotoxins obtained from *Escherichia coli* and *Salm. abortus equi.* Over 10 gamma of purified endotoxins may liberate histamine from rat subcutaneous tissue; this phenomenon does not occur in animals rendered tolerant to the endotoxins. The action of cotton extracts is similar to that of purified endotoxins, but in their case even endotoxin tolerant animals show activity; this is probably due to the simultaneous presence of other histamine liberating substances."

G. F. Keatinge

ZWETKOFF, L. Die unspezifische Allergie und die experimentelle Tuberkuloseinfektion. [**Non-Specific Allergy and Experimental Tuberculosis**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1961, Feb., v. 7, No. 2, 134–40, 3 figs.

A previous investigation had shown that, of 100 sick cotton textile workers, 62·2% suffer from diseases of the respiratory passages and 37·8% from other diseases. Of the respiratory conditions, bronchitis was the most common, tuberculosis less common and asthma still less common.

Cotton dust renders the body hypersensitive and this hypersensitivity is more marked with cotton containing seed than with purified cotton. There may be several types of cotton allergy. Cotton contains organic and inorganic materials, such as proteins from seeds, bacteria, spores of moulds, etc., and a small amount (0·27 to 1·8%) of silica.

The present experiments, from Sofia, were designed to test the effect of this non-specific allergy on the course of tuberculosis. Guineapigs were selected because the rapidity of progression of tuberculosis resulting from the injection of varying lethal doses has been ascertained in this animal.

Two sets of experiments were performed. In the first series 4 guineapigs were injected daily for 8 to 14 days with cotton extract totalling 9 to 50·5 cc. The animals were then infected subcutaneously with 0·5 mgm. emulsion of tubercule bacilli (20 million). All 3 controls died within 137 days, 3 of the tested animals survived up to 171 days.

In the second series 10 guineapigs were tested: there were 4 controls. Two of each died of the intercurrent disease. The test animals were given 1 cc. extract of

cotton daily for 118 days and then injected with 1·0 mgm. tubercule bacilli emulsion (40 million). The test animals survived 30·4 days, the controls 34 days.

It is considered that the results show that the weaker infection and shorter duration to cotton treatment delays the development of experimental tuberculosis while massive infection and a longer and stronger allergizing exposure hastened the development of the tuberculosis. These results conform to the results of investigation into the progression of tuberculosis in cotton workers in Bulgaria. *Charles L. Sutherland*

ODELSCALCHI, C. P. & STRANEO, G. Dosaggio colorimetrico e polarografico del piombo atmosferico raccolto su filtro cellulosico. [**Colorimetric and Polarographic Dosage of Atmospheric Lead collected on Celluloid Filters**] *Rass. Med. Indust.* Rome. 1960, Sept.–Oct., v. 29, No. 5, 356–61, 1 fig. & 1 diagram. English summary (3 lines).

Measurement of toxic fumes in the atmosphere is a problem of outstanding interest in the field of occupational hygiene and preventive medicine and nowadays colorimetric tests enable quick and accurate assessments to be made of many commonly used substances. However, it is only recently that rapid measurements of the concentrations of metal fumes in the atmosphere have been possible and Mines Safety Appliances (MSA) have now made available the "Lead in Air" detector which provides a means for the prompt assessment of concentrations of lead in the atmosphere. The apparatus consists of a hand-operated pump which at each stroke draws fixed amounts of air across a cellulose filter treated with appropriate reagents. If lead is present a rose colour appears and on the basis of the number of strokes of the pump and the intensity of the colour reaction it is possible by comparison with a colorimetric scale to check speedily and directly the amount of lead present in the sample of air examined.

The results thus obtained were compared with those determined by polarographic examination of fume aspirated on to a cellulose filter by means of the "Fixt-Flo" air sampler. A detailed formula for the calculation of the lead concentration is given. The choice of this air sampler was made because of the simplicity and flexibility of the aspirator which permits three rates of flow enabling the amount of air aspirated to be varied in accordance with the presumed degree of pollution and also because the air flow is constant whatever the length of time for which it is continued. As an additional check, samples of the vitiated air were taken under the same conditions with an impinger according to the recommendations and method of the American Conference of Industrial Hygienists of 1958. It is generally held that a determination within 10% of the maximum allowable concentration is acceptable and both the "lead in air" test and that carried out with the "Fixt-Flo" air sampler gave determinations of greater exactitude.

The results obtained by all three methods showed a good correlation and it is concluded: (1) That the quantitative determination of atmospheric lead in air collected with a cellulose filter is an efficient means for the purpose already indicated. (2) Colorimetric assessment with the reagents recommended in the "lead in air" tests of MSA is acceptable and does not present appreciable discrepancies compared with the values obtained by other methods. (3) Polarographic determination of the lead collected on cellulose filter enables quite precise measurement to be made and in addition the results can be plotted as a graph which is clearly important especially when there are associated medico-legal considerations. Collection of the polluted atmosphere on cellulose filter also allows the filter to be sent to polarographic laboratories for a rapid, exact, documented assessment. *G. F. Keatinge*

DE BRUIN, J. De dosering van Ca-EDTA bij de behandeling van chronische loodintoxicatie. [**Ca-EDTA dosage in the Treatment of Chronic Lead Poisoning**] *Nederl. Tijdschr. v. Geneesk.* 1961, Mar. 11, v. 105, No. 10,. 482–4, 1 chart. English summary (9 lines).

As the result of reports that Ca-EDTA, in daily doses ranging from 4–40 gm., had nephrotoxic effects [this *Bulletin*, 1957, v. 32, 870, 1171], the author, with experience of 60 cases of lead poisoning, tried doses up to 2·65 gm. (for an adult weighing 75 kgm.).

Evaluating his experience and the evidence of the effect of this treatment on the metabolism of lead, he decided to alter the administration.

He found that his cases (16) responded rapidly and well to the use of 2·65 gm. by intravenous injection on alternate days.

One illustrative cases is described, where treatment was continued for 52 days. It is advised that treatment should be continued until the urinary lead excretion level reaches a normal level of 100–300 μgm., by which time symptoms and signs will have been absent for some time and the blood picture returned to normal.

It is considered that treatment in this way is both safe and certain. *Kurt Schwarz*

DIZON, G. D., ANSELMO, J. E. & VILLANUEVA, J. Examen del riesgo en una mina de mercurio de Filipinas. [**Examination of the Risk in a Mercury Mine in the Philippines**] *Med. y Seguridad del Trabajo.* Madrid. 1960, July–Sept., v. 8, No. 31, 29–36, 1 chart. English summary (9 lines).

After a brief reference to the history of the mining of mercury and the part of the world in which it has been found, it is stated that the metal has only been exploited in the Philippines in recent years. The methods in use, which are largely mechanized, are described in the text and also shown in the form of a flow chart. The concentration of mercury vapour present in the various parts of the refinery was estimated by means of the Kruger mercury vapour meter and the results are presented in a table where the concentration is expressed in mgm. per cu. m. giving maximum and minimum figures. Most of the maximum figures were higher than the maximum permissible concentration of 0·1 mgm. per cu. m. of air.

151 workmen are employed and all except 5, who were absent from work at the time of the investigation, were examined. The examination included a search for oral signs, muscular tremor, erethism and emotional instability, irritability, restlessness or other evidence of nervous involvement. 20 of those examined had pyorrhoea, 9 showed slight loosening of some teeth: 16 had tremor of the fingers noted on writing their names: 14 complained of irritability, 3 of restlessness, and 15 of slight loss of weight. Tremor, erethism or emotional instability are regarded as the principal manifestations of chronic mercury poisoning as a result of exposure to vapour and among the workers engaged in grinding operations where the concentration of mercury vapour was from 0·1 to 0·4 mgm. of 11 workmen 3 showed slight trembling of the fingers, 2 complained of irritability and 1 of restlessness. On the other hand elsewhere with a concentration of 0·1 to 0·2 mgm. of 6 workmen none showed tremor or emotional instability.

The management was aware of the risks involved and had taken steps in the matter including the provision of breathing apparatus and routine estimations of mercury in the urine: if in any man more than 100 mgm. per 100 cc. urine were excreted in the day, admission to hospital for closer observation was arranged. The presence of mercury in the urine is regarded by the authors as no more than a guide to the amount absorbed. Despite the findings recorded in this paper, the conclusion is reached that no certainty of chronic mercury poisoning had been established among the workers examined. *G. F. Keatinge*

Tolot, F., Neulat, G. & Mallein. Une observation de leucose myéloïde due aux hydrocarbures benzéniques. Grande latence initiale; surveillance hématologique montrant les phases d'installation de la leucose. [**A Case of Myeloid Leucosis due to Aromatic Hydrocarbons. Long Initial Dormancy; Haematological Supervision Showing Stages in the Establishment of the Leucosis**] *Arch. Malad. Professionnelles.* Paris. 1961, Mar., v. 22, No. 3, 159–61.

A heliogravure press operator had normal 6-monthly blood counts, from 1945, when he began work with solvents containing among other substances benzene or a homologue, until 1956 with one exception in 1950 when white cells numbered 10,500 and red cells 3·6 million. In 1956 white cells repeatedly were about 12,000 and 1 year later 16,400 with 4% myelocytes. The marrow count showed only moderate increase of granulocytes. Hospital investigations were otherwise negative. The man's work was changed away from solvents and the condition remained stationary until 1959. Then slight anaemia developed and the white cells increased to 300,000 with 44% young-form myelocytes. After treatment they decreased. In 1960 the blood contained 3·9 million red cells, 18,800 white cells and 750,000 platelets. The spleen was never enlarged.

In 1945 the use of benzene ceased in this printing establishment because of cases of poisoning, 1 fatal. From then until 1952 the solvent contained 5% benzene, 20% toluene and 75% essence C and afterwards 10% cyclohexane, 15% toluene and 75% essence E, the essences being derivatives of petrol and cyclohexane. It was concluded that exposure to small amounts of benzene homologue was responsible for the hyperplasia. A leucocytosis above 10,000, in the absence of infection and which persists at 3 monthly examinations indicates the need for removal from exposure temporarily at least. *M. Patricia Fitzsimons*

Gramer, L. Über die Problematik der Methoden zur Bestimmung von Kohlenoxyd im Blut (Vergleichende Untersuchungen). [**Criticism and Comparison of Methods for the Determination of Carbon Monoxide in Blood**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1961, Mar., v. 11, No. 3, 53–9, 17 figs. [Numerous refs.]

This paper is based on an experience of about 800 blood samples which in the course of years have been submitted for examination.

The author stresses the need for careful and accurate blood sampling before discussing the quantitative methods of determining the carbon monoxide concentration which are in use, their accuracy and most frequent sources of error. There is much technical detail in this short paper with its numerous references in which there are also suggestions for the modification and improvement of accepted methods of analysis and the development of new procedures. Some details are also given of the method at present in use in the Institute of Industrial Medicine of the Saarland University of Saarbrücken. *M. E. Delafield*

Lawson, D. D., McAllister, R. A. & Smith, G. **Treatment of Acute Experimental Carbon-Monoxide Poisoning with Oxygen under Pressure.** *Lancet.* 1961, Apr. 15, 800–802, 2 figs.

Oxygen at 2 atmospheres pressure revived or protected rodents and in dogs comparative tests showed it to be most rapid in lowering carboxyhaemoglobin. Artificial respiration with oxygen at this pressure was previously reported as successful in persons poisoned by CO.

Groups of 12 rats and 3 cavies were exposed in a pressure vessel to 3% CO in air. Group A quickly became ataxic and unconscious and died in 3–15 minutes. When in the next experiment Group B became unconscious oxygen was admitted to raise the pressure to 15 pounds per sq. inch above atmospheric pressure. These animals recovered consciousness in 1–3 minutes though the CO was still present. They were decompressed 10–15 minutes later. Group C, to which the oxygen was admitted with the CO, remained conscious and behaved normally for periods up to 3 hours when they were decompressed. Group B and C behaved normally when removed from the vessel and did not lose consciousness, suggesting that simple solution of oxygen in plasma was not the only protective factor. This was confirmed by blood analysis in 5 rats and 2 cavies from each group immediately after being killed

or in Group A after death. The oxygen carried by haemoglobin in B and C was twice that in A.

Human and equine blood samples, exposed *in vitro* to coal-gas, are shown graphically to lose CO slowly when filmed in air, faster in 1 atmosphere of O_2 and fastest in 2 atmospheres of O_2.

After breathing CO and O_2 through a cuffed intratracheal tube for 1–2 hours until respiratory depression occurred, 4 dogs were made to inspire air, oxygen or 5% carbogen by means of an artificial respirator. Serial blood samples were withdrawn from the right atrium. The curves of results show carboxyhaemoglobin falling from 80% to 15% in 20 minutes with the 2-atmospheres oxygen and taking 40 minutes approximately with the 1-atmosphere oxygen and the carbogen, the latter being slightly the quicker; the air curve took 40 minutes to reach 40%. *M. Patricia Fitzsimons*

PAULET, G. Nouvelles perspectives dans le traitement de l'intoxication cyanhydrique. [**New Views on Treatment in Hydrocyanic Poisoning**] *Arch. Malad. Professionnelles.* Paris. 1961, Mar., v. 22, No. 3, 120–27, 1 fig.

A review of stages in the treatment of cyanide poisoning leads to the place of organic cobalt compounds. Experiments with dogs, rabbits, guineapigs and mice are described or discussed which show the rapid antidotal effect of 2 cobalt chelates. Reasons are given to show why in severe poisoning—instead of nitrite-thiosulphate treatment—$EDTACo_2$ should be injected intravenously and followed by hypertonic glucose solution, while artificial respiration and oxygen administration is continued. The toxicity of $EDTACo_2$ itself is lessened in the presence of cyanide and of the glucose solution which also aids distribution.

A kymograph reproduction shows respiratory and blood pressure changes in the anaesthetized dog when NaCN is injected intravenously in a dose of 0·1 mgm. CN per kgm. per minute; breathing stops after about 8·5 minutes; the perfusion is stopped; later, after a short period of gasping, secondary apnoea occurs and the animal dies. Injection of the chelates during secondary apnoea restores respiration and blood pressure. They were the only substances tested to do this. In experiments lasting some hours, no changes took place when cyanide and antidote were injected simultaneously; the 0·1 mgm. per kgm. CN was neutralized by 0·8 mgm. $EDTACo_2$ per kgm. or by 1·2 mgm. per kgm. of histidine cobalt.

Dogs during secondary apnoea and rabbits when breathing stopped after intramuscular injection of 4 or 5 mgm. NaCN per kgm. were injected intravenously with 20 mgm. $EDTACo_2$ per kgm. and 10 of 12 dogs rapidly recovered and 83% of rabbits. Similarly, 30 mgm. per kgm. histidine cobalt saved 88% rabbits but only 57% were saved by sodium nitrite and thiosulphate, 15 and 500 mgm. per kgm.

Inhalation poisoning by HCN was treated in 69 dogs when breathing stopped. After the antidote, glucose solution was injected intravenously and when breathing did not start in 1 minute artificial respiration was given. Survival rates when this was necessary were: with nitrite-thiosulphate, 15 and 200 mgm. per kgm., 0%; with histidine cobalt, 45 mgm. per kgm., 54%; with $EDTACo_2$, 25 mgm. per kgm., 60%. Total survival rates with these 3 were respectively 27%, 60% and 71%, and 62% survived with 12–20 mgm. $EDTACo_2$ per kgm., with or without aided respiration.

Mouse LD50 are recorded: intravenously, $EDTACo_2$, alone 50, in the presence of 2·5 or 5 mgm. NaCN per kgm., 82 or 103 and with 20% glucose, 150; intraperitoneally 213; histidine cobalt and sodium nitrite intraperitoneally 290 and 193; figures are mgm. per kgm. A dose of 600 mgm. $EDTACo_2$ in glucose solution, followed by 50 ml. glucose solution through the same intravenous needle is suggested, if a poisoned subject is too far gone for nitrite-thiosulphate treatment [this *Bulletin*, 1961, v. 36, 537]. *M. Patricia Fitzsimons*

COPE, C. **The Importance of Oxygen in the Treatment of Cyanide Poisoning.** *J. Amer. Med. Ass.* 1961, Mar. 25, v. 175, No. 12, 1061–4, 2 figs. [11 refs.]

Experiments are quoted and described to show that oxygen is not only important—the natural intracellular antidote and first defence line—but should be administered as a specific antidote in the immediate treatment of all forms of cyanide poisoning. It should be accompanied, when necessary, by artificial respiration, vasopressor agents or cardiac massage and, especially in skin or oral poisoning, by the nitrite—thiosulphate injections, the second defence line for aiding detoxification, binding and excretion, as well as by washing the skin or gastric lavage. [See this *Bulletin*, 1961, v. 36, 537; see also above.] Nitrite-thiosulphate therapy shortens the course of intoxication, lessening the likelihood of cerebral damage. Amyl nitrite inhalation is relatively ineffective in producing methaemoglobin, and carbon dioxide is not necessary because cyanide is a powerful respiratory stimulant.

After inhalation poisoning, if breathing and blood pressure are adequate, the subject will probably recover without further treatment. As long as the normal blood oxygen tension of 100 mm. is maintained it will exert protection. Cyanide hyperventilation in the normal subject can raise the tension to 110–120 mm. However, subjects with heart, lung or cerebral artery disease are probably functioning at borderline tension and may die before treatment. They should not work where cyanide accidents are possible.

A high tension of oxygen can block the respiratory gasp reaction to intravenous cyanide in man and protect goldfish from lethal doses, and electrocardiographic tracings show that it can partially reverse anoxic changes in poisoned dogs. In Russian experiments early continuous inhalation of 2·5 atmospheres of oxygen protected most mice from lethal doses. PAULET showed that oxygen saved dogs in late stages of poisoning and that even when heart and blood pressure begin to fail survival will occur if carotid pressure is maintained by perfusion of the animal's blood (*Presse Méd.*, 1957, v. 65, 573; *C. R. Soc. Biol.*, 1954, v. 148, 1009).

M. Patricia Fitzsimons

JOYNER, R. E. & PEGUES, W. L. **A Health Hazard associated with Epoxy Resin-Concrete Dust.** *J. Occup. Med.* Chicago. 1961, Apr., v. 3, No. 4, 211–14.

Inhalation of dust or vapour or both caused illness in 6 men among a team of 8 while engaged in destroying an epoxy resin-concrete foundation with air-impact hammers under a light stream of water. A fume was visible and an odour resembling xylene was noted. The hardener in this cold-cured resin was a mixture of triethylenetetramine and dimethylaminopropylamine, and the resin-concrete was so impervious that release of xylene, a constituent of the resin precursors, was considered plausible on tooling, even 18 months after the concrete was laid. The illness, which was different from polymer fume fever, showed itself by headache, sore throat and irritating cough and the urine, for a time, contained albumin and red and white blood cells. Secondary infection followed in some of the patients. The men had worn goggles and when air-supply respirators were provided the patients were able to finish the 5-days job. Later, similar jobs were done without mishap when dust respirators were used.

Laboratory investigations were carried out on resin-concrete samples which were ground, drilled or pyrolyzed to simulate working conditions. There was no release of epichlorhydrin, other aromatic chlorine compounds, free amines or alkaline material. The vapour was composed of 90% xylene, an unidentified thermal resin decomposition product and small amounts of chlorine compounds, probably from hydrochloride salts of amines. Nitrogen compounds were found in the dust. This probably acted as a carrier for amine salts which were believed to be present, and amine hydrochlorides would dissolve on mucous surfaces.

The respiratory irritation and the effect on the kidneys may have been due to the xylene alone, or to unknown resin decomposition products [see also this *Bulletin*, 1959, v. 34, 913]. *M. Patricia Fitzsimons*

HIFT, W. & PATEL, P. L. **Acute Acetone Poisoning due to a Synthetic Plaster Cast, with a Discussion of Acetone Metabolism.** *South African Med. J.* 1961, Mar. 25, v. 35, No. 12, 246–50, 1 fig. [20 refs.]

Biochemical findings in this case of a boy aged 7 are discussed together with 8 previously recorded reports of poisoning after application of similar casts. The boy was in good health, with only a raised erythrocyte sedimentation rate left after treatment for 3 months for osteomyelitis complicated by meningitis, pericarditis and infective synovitis. His plaster of Paris spica was then replaced by a plaster substitute consisting of glass and textile bandages, set, under a ventilating fan, by means of a fluid composed chiefly of acetone. Acetone poisoning showed itself 6 hours later and recovery took 3–4 days. The cast was not removed and treatment was symptomatic, with no glucose or insulin.

Drowsiness, restlessness, sweating and pain over stomach and bladder were quickly followed by repeated vomiting of altered blood, intense thirst and tachycardia, deep sighing and irregular respirations, nystagmus, clumsy hand movements and poorly reacting pupils when illuminated from 1 side. There was acetone in the breath. The urine contained acetone, diacetic acid, occasionally albumin and on the first day, sugar. Dehydration was not severe. Serum chlorides were low. Blood sugar and cerebrospinal fluid sugar were raised. The alkali reserve was normal, and so were serum lipids and cholesterol. Acetone sensitivity tests were negative. The glucose tolerance test a fortnight later, with a fasting level of 49 mgm. per 100 ml., after intravenous injection of 25 gm. glucose gave half-hour values of 225, 105, 49, 31 and 40 mgm. per 100 ml., and 2 months later, after 12·5 gm. the levels were (fasting 84) 184, 115, 76, 84 and 100, with glycosuria on both occasions, after 1 hour.

Diabetic coma, not surprisingly, had been diagnosed at one stage in some of the cases, and some symptoms in this disease may be due, in part at least, to endogenously formed acetone. Acetone can be absorbed through lungs or skin or both and can be metabolized to carbon dioxide, aceto-acetic acid, saccharides and possibly lipids. *M. Patricia Fitzsimons*

FEINSILVER, L., PERREGRINO, J., ROSS, M. A., YEVICH, P. P., STOUFER, R. M. & OBERST, F. W. **The Acute Inhalation Toxicity of Heated Aerosols of Three Hydraulic Fluids.** *Amer. Indust. Hyg. Ass. J.* 1961, Feb., v. 22, No. 1, 14–20, 1 fig. [16 refs.]

Owing to the development of new and more powerful aircraft engines operating at higher temperatures, it has become necessary to study the behaviour of some organic compounds which come into contact with heated metal surfaces. It may be that under conditions of operation at high temperatures toxic products may be generated by pyrolysis of lubricants and hydraulic fluids.

This paper describes acute toxic effects in animals that inhaled the airborne products resulting from the pyrolysis of 3 hydraulic fluids at temperatures of 520°, 1020° and 1560°F. The fluids tested were: (i) OS-40, a phosphate ester; (ii) XF-408, a mixture of silicone oil and a fluorochlorohydrocarbon; and (iii) MLO-5277, an organo-silicate. The methods of test are fully described. The fluids were dispersed as aerosols, and the experimental animals were rats and dogs.

Several decomposition products of each fluid were selected for quantitative determination in the air of the test chamber. Those from OS-40 included inorganic phosphate, phenols, total aldehydes and carbon monoxide. For XF-408 inorganic chloride, inorganic fluoride, total aldehydes and carbon monoxide were determined; and for MLO-5277 measurements of carbon monoxide and total aldehydes were made.

The aerosols, whether heated or not, were irritants to the eyes and respiratory tract. The toxicity was generally proportional to the nominal concentration of the aerosol and to the temperature to which the aerosol was subjected, except in the case of dogs exposed to XF-408. Aerosols of this fluid, unheated and heated at 520°F., caused acute tubular nephrosis, but this lesion was not observed in dogs exposed to the aerosol heated

at 1020° or at 1560°F., although the incidence of deaths was greatest after exposure to the aerosol heated at 1560°F.

OS-40 produced severe changes in rats and dogs only when the nominal concentration of the fluid heated to 1560°F. was 3·5 to 4·3 mgm. per litre. The toxicity of OS-40 varied with the degree of decomposition and with the concentration of aldehydes and carbon monoxide formed as the result of heating. The maximum effects were produced with heating to 1560°F.

On the basis of the response of animals exposed to the unheated fluid and to low concentrations of the pyrolyzed fluid MLO-5277 was considered the most toxic of the 3 fluids studied. Pyrolysis at 1020° and at 1560°F. produced low concentrations of carbon monoxide and aldehydes which could not account for the high mortality observed, and the responsible toxic degradation product was not identified.

OS-40 was regarded as the least toxic of the 3 fluids.

Thomas Bedford

SVIRBELY, J. L., DOBROGORSKI, Olga J. & STOKINGER, H. E. **Enhanced Toxicity of Ozone-Hydrogen Peroxide Mixtures.** *Amer. Indust. Hyg. Ass. J.* 1961, Feb., v. 22, No. 1, 21–6. [15 refs.]

The authors have studied the interactions of common air-polluting substances, chiefly respiratory irritants, with ozone, in order to ascertain whether or not the degree of injury observed in animals could be attributed to a possible potentiation of combinations of those irritants. The present paper describes the results of tests made with ozone-hydrogen-peroxide mixtures. The acute and subacute lethal effects of such mixtures; the spread of tolerance, observable with ozone, to hydrogen peroxide; and the cross-tolerance to either component following brief exposures to non-lethal levels of the other, were investigated. Rats, mice and hamsters were used as experimental animals, and they were exposed for 4-hour periods.

Hydrogen peroxide, in concentrations of 3·3 p.p.m. and above, enhanced the toxic effects of usually non-injurious doses of ozone (about 1 p.p.m.) in mice, while concentrations of 7·8 p.p.m. or more of hydrogen peroxide were required to produce the same effect in rats.

An initial exposure to hydrogen peroxide at about 0·2 LD50 concentration gave mice a moderate degree of protection against otherwise lethal doses of hydrogen peroxide.

Repeated exposure of mice to low levels of hydrogen peroxide, or a single exposure to about 0·2 of a lethal dose, can confer tolerance to what would otherwise be a lethal dose of ozone.

Thomas Bedford

LONG, J. E. & HATCH, T. F. **A Method for assessing the Physiological Impairment produced by Low-Level Exposure to Pulmonary Irritants.** *Amer. Indust. Hyg. Ass. J.* 1961, Feb., v. 22, No. 1, 6–13, 10 figs.

Pulmonary oedema is the characteristic state produced by irritant gases of low solubility which are significantly absorbed from the inhaled air only in the lungs. The oedema may progress to a fairly advanced state before discomfort is caused or signs of disturbance, as revealed by common indices of pulmonary performance, are evident. There is need for a sensitive method of assessing early pulmonary changes before serious psychological impairment, or even subjective discomfort, is produced.

The earliest physiological consequence of pulmonary oedema is an increase in the resistance to the diffusion of gas across the pulmonary membrane. Even in minimal amount oedema must obstruct diffusion to a measureable extent. The proposed method of test involves measurement of the rate of respiratory absorption of carbon monoxide, which is a function of both the rate of effective lung ventilation and pulmonary diffusion capacity. In the healthy animal at rest the rate of absorption of carbon monoxide is determined mainly by the rate of lung ventilation, but with the onset of oedema the reduced capacity for diffusion becomes increasingly important and will, if sufficiently reduced, become the limiting factor in determining the rate of absorption.

The closed-circuit respirometer and the test procedure used in the experiments are described.

Measurable degrees of pulmonary impairment were demonstrated in unanaesthetized rats following 30-minute exposures to concentrations of phosgene ranging from 5 to less that 1 p.p.m. Measurable reductions in the rate of absorption of carbon monoxide were found in animals the lungs of which could not be distinguished histologically from those of unexposed animals.

Thomas Bedford

MILLER, B. H., NAVONE, R. & OTA, M. **Irritation from Residual Bromides after Methyl Bromide Fumigation.** *Pub. Health Rep.* Wash. 1961, Mar., v. 76, No. 3, 216–18.

Pilot lights should not be forgotten when, as instructions demand, flames are extinguished before fumigation with methyl bromide. After a house had been aired, which would have removed all the methyl bromide, members of the household were eventually driven to sleeping in a tent because of irritation of eyes, nose, throat and skin which persisted for some time. Enquiry revealed similar complaints, and in some houses stoves and metallic objects were corroded after fumigation. Laboratory tests with various bromides indicated that hydrobromic acid can react with fabrics, wood and metals to form bromides, whereas methyl bromide cannot.

Tests were carried out in fumigated houses. Samples were obtained by wiping about 200 square inches of surfaces with paper impregnated with 1% sodium bicarbonate solution. Analyses of samples showed a maximum of 0·06 mgm. bromide per sample in houses where no light was burning and 0·23–0·75 mgm. where a pilot light was left burning. In the latter group, 1 house had 0·84–2·2 mgm. 4–6 months after fumigation, and here irritation of the skin had been reported. After the surfaces were washed, no bromide was detected.

It was calculated that the usual 1·5% concentration

of methyl bromide could in the presence of a gas flame decompose to form 72 p.p.m. hydrogen bromide; the MAC is 5 p.p.m. If after fumigation metallic objects are corroded or if irritation is experienced, all exposed surfaces and fabrics should be washed with a mild alkaline solution. *M. Patricia Fitzsimons*

AMDUR, Mary O. **The Respiratory Response of Guinea Pigs to the Inhalation of Acetic Acid Vapor.** *Amer. Indust. Hyg. Ass. J.* 1961, Feb., v. 22, No. 1, 1–5, 4 figs.

Acetic acid is used in various industrial processes. Its vapour is irritating to the eyes and the mucous membranes of the respiratory tract. The suggested maximum allowable concentration of acetic acid in industrial atmospheres is 10 parts per million (p.p.m.) of air.

In the present paper the author reports the effects on the lungs of unanaesthetized guineapigs of exposures to acetic acid vapour at concentrations ranging from 5 to 500 p.p.m. for periods of 1 hour.

The 3 physiological measurements made were the intrapleural pressure, the tidal volume, and the rate of flow of gas into and out of the respiratory system. Simultaneous recordings were made of these measurements. The flow-resistance of the lungs and airway was calculated by relating the change in intrapleural pressure to the change in the flow rate between inspiratory and expiratory points on the tracing corresponding to equal lung volumes. The "compliance" ($\Delta V/\Delta P$, ml./cm.H_2O) was calculated by relating the tidal volume to the intrapleural pressure change at the beginning and end of expiration. Each animal served as its own control.

At all the concentrations studied there was an increase in the resistance accompanied by a slight decrease in compliance. The product of resistance and compliance, or the time constant of the lungs, increased during exposure at all the concentrations studied. All these changes were statistically significant.

Acetic acid also caused a decrease in the respiratory rate and the minute volume, but these changes were statistically significant only at concentrations of 120 or more p.p.m.

It is concluded that the primary effect of acetic acid vapour is probably bronchial constriction, and the overall picture is similar to that observed with other irritant gases and vapours. The presence of a sodium chloride aerosol delays recovery but does not increase the magnitude of the response observed.

Thomas Bedford

MURATA, S. [**An Experimental Study on the Toxicity of Triorthocresyl Phosphate**] *Igaku Kenkyu.* Fukuoka. 1960, Dec., v. 30, No. 12, 3388–400, 18 figs. [11 refs.] [In Japanese.] English summary.

Triorthocresyl phosphate is well known as a cause of poisoning by ingestion. The author determined its LD50 for mice at 4·64 gm. per kgm. body weight. He describes the clinical effects in mice, which include (after ingestion) severe inflamatory changes in the gastro-intestinal tract, haemorrhagic necrosis of the liver, desquamation and haemorrhage of the epithelium of the tubules of the kidneys, with atrophy of the glomeruli, and congestion and haemorrhage of the lungs. [This is condensed from the English summary.]

Charles Wilcocks

REEDER, D. H. **Organic Phosphate Insecticide Poisoning.** *J. Occup. Med.* Chicago. 1961, Mar., v. 3, No. 3, 129–30.

Respirators and clothing adequate for routine work of adding tetraethylpyrophosphate (TEPP) to agricultural dusting powders did not protect when the mixing mill became clogged after 10 times the amount of TEPP had been added in error. A few hours after entering the mill to remove the mixture which had become gummy, 2 men, aged 23 and 42, became ill. Clothing was stripped, the body washed and each man given 2 mgm. atropine by mouth. Hospital case reports show that it took some 9 hours' treatment with intravenous atropine before the pupils dilated and began to react and before the older man's moist chest signs cleared. Disorientation, confusion and restlessness necessitating restraint developed. After further treatment recovery was complete in 3 days.

Meanwhile plasma cholinesterase determinations were made by means of a *p*H meter, and the values are expressed as *p*H change per hour, the normal range being 0·25–1·36. Shortly after symptoms began the values were 0·308 and 0·525; 1 month later they were 0·75 and 0·84. In a plant where phosphate esters are handled continuously the values vary from 0·65 to 1·25 and 0·5 is considered the danger level (red cell cholinesterase values vary from 0·72–0·99 in this plant).

The younger patient had 1·2 mgm. atropine intravenously each hour for 8 hours, then 0·6 mgm. every 2 hours for 6 hours and 8 hours later 0·4 mgm.; the older had 1·3 mgm. hourly for 14 hours.

M. Patricia Fitzsimons

MALINAK, L. R., DERBES, V. J. & LIENHARD, W. F. **The Effects of Sodium Fluosilicate, Na_2SiF_6 on the Skin and Eyes of Rabbits.** *J. Investigative Dermat.* 1961, Mar., v. 36, No. 3, 183–8, 8 figs.

The authors report some experiments on the effect of the insecticide and fungicide sodium fluosilicate, Na_2SiF_6, on rabbit skin following the observation of lesions of previously traumatized skin in workers exposed to this compound. The compound had no effect on the intact skin, undamaged eye or eye damaged by a scratch of the cornea, in the rabbit. When the compound was applied to superficial scratches in the skin necrotic lesions developed provided the material was in contact with the skin for more than 2 minutes. Similar lesions were produced by injecting 0·1 ml. of a saturated solution of Na_2SiF_6 intradermally or just below the skin. The lesions took 12–14 days to heal.

H. B. Stoner

MEDICAL RESEARCH COUNCIL. **Introductory Manual on the Control of Health Hazards from Radioactive Materials. Committee on Protection against Ionizing Radiations.** *Med. Res. Council Memorandum No. 39.* pp. vi + 21. [24 refs.] 1961. London: H.M. Stationery Office. [1s. 9d.]

There was an issue under this title in 1949. It was reprinted 6 times between 1949 and 1954. The present issue is an extensively revised edition.

This is intended mainly for the guidance in outline of those concerned with the manipulation of radioactive materials in laboratories and elsewhere.

The recommendations on maximum permissible doses of external and internal radiation and concentrations of radioisotopes in air and in water are based on those of the International Commission on Radiological Protection, published in 1959, and of its Committee on Permissible Dose for Internal Radiation, published in 1960, as well as on those of the Councils Committee on Protection against Ionizing Radiation. It is stated in the preface that as the views of these two bodies do not at present completely correspond in all respects, the memorandum expresses the British views based on the most up-to-date information available.

Every aspect of the subject appears to be covered in this valuable memorandum. It covers the methods of measurement and the permissible doses of radiation under many working conditions. Laboratories are discussed under headings Grade C, B and A according to the grade of hazard. Protective clothing and the methods of dealing with contamination contain a great deal of valuable information. It is sometimes a very difficult matter to rid the hands of radioactive material. Scrubbing with soap and water is not always effective and recourse may be had to titanium dioxide paste, or a saturated solution of potassium permanganate followed by a rinse of 5% sodium bisulphate. Great care must be taken to avoid abrasions if any sort of nail brush is used.

Disposal of radioactive waste remains a problem to be solved in differing ways according to whether the unwanted material is solid, liquid or gaseous.

There is an Appendix which gives the thicknesses of various materials required to halve the intensity of an incident beam of gamma rays ranging from 0·3 to 3·0 MeV.

The whole memorandum should prove of outstanding importance to all engaged in radioactive handling.

S. Russ

KITABATAKE, T. **Sterility, Stillbirth, Infant Death, and Sex Ratio of Offsprings of X-Ray Workers.** *Nagoya J. Med. Sci.* 1960, Dec., v. 23, No. 3, 227–37, 2 figs. [40 refs.]

This investigation was carried out among married males in the Aichi Prefecture of Japan by means of questionnaires addressed to 243 X-ray workers (40 radiologists, 203 technicians) and a control group of 260 employees of a local industrial establishment with no radiation hazard. Both groups were asked to provide marriage histories which included details of all pregnancies of their wives, while X-ray workers alone were further questioned as to the nature and duration of their occupational exposure to radiation. Usable replies were received from 137 (56·4%) of persons in the radiation group and 140 (53·8%) members of the control group.

The replies received were analysed to compare the groups with respect to incidence of sterility, miscarriage, stillbirths, infant deaths and the sex-ratio of their offsprings. Differences between them were confined to the incidence of primary sterility, defined as no pregnancy within 5 years of marriage, and sex-ratio of offsprings. Primary sterility was recorded for 20·5% of the 102 X-ray workers who had been married for more than 5 years and for only 5·5% of 91 non-radiation workers married for the same length of time. Again the proportion of males (53·3%) among 246 children of the radiation group was higher than the comparable proportion (50·9%) among 287 offspring of the control subjects. Both these differences were technically significant. [In view of the small size of population surveyed and the relatively low response-rate achieved, the comparisons presented in this study should, perhaps, be interpreted with some caution.] *J. T. Boyd*

J. OCCUP. MED. Chicago. 1961, Mar., v. 3, No. 3, 145–92, 10 figs. & 2 coloured pls. [58 refs.] **Acute Radiation Death resulting from an Accidental Nuclear Critical Excursion.**

The accident occurred at the Los Alamos Scientific Laboratory U.S.A. on December 30, 1958. A man died as result; he was in charge of the controls in a chemical process for the recovery of plutonium. Without any warning a critical reaction was reached, an enormous outburst of neutron and gamma rays took place. The man received this and instantly was profoundly shocked; all he could say to his rescuers was "I'm burning up". He died in 35 hours. The present symposium consists of eight sections dealing with various aspects of this happening; they will be dealt with seriatim. The victim is referred to as K.

Description of the accident and subsequent events (pp. 147–149) by T. L. SHIPMAN. The accident occurred where "lean" residues of waste material in solutions containing less than 0·1 gm. Pu per litre were processed. This was a routine operation which had been carried out many times for a number of years; it was implicit in the system of operations that the tanks could not contain enough Pu at any one time to permit a critical reaction. But it was subsequently found that plutonium-rich solids, that normally would have been handled separately, were washed from 2 tanks into a large vessel that contained dilute aqueous and organic solutions. Most of the aqueous solution was removed from this vessel; then the remaining 40 gal. of material were transferred to a stainless steel solvent-treating tank which already contained about 80 gal. of emulsion that had resulted from another step in the recovery process. The mixture was over-rich.

Clinical course of case K (pp. 150–154) by C. C. LUSHBAUGH. The course of events is divided into 4 periods. The first period (20–30 minutes) was characterized by K's physical collapse and mental incapacitation which progressed to semi-consciousness and severe prostration. The second period (1–1½ hours) began with his arrival by stretcher and ended with his transfer to the ward; this period was characterized by such severe cardio-vascular shock that death seemed imminent. The third period was about 24 hours in which there was enough subjective improvement to encourage continued attempts to alleviate his anoxia, hypertension and circulatory failure. The fourth period began with the unheralded onset of rapidly increasing irritability and uncooperativeness, bordering on mania, followed by coma and death in about 2 hours.

Clinical pathology and biochemistry (pp. 155–159) by D. F. PETERSEN. A number of tests were carried out upon the limited amount of material available. In the main these were upon serum enzymes, urinary constituents, serum proteins and serum antibodies.

Gross and microscopic pathology and neuropathology (pp. 160–168) by C. C. LUSHBAUGH. Here is a very complete account of the post-mortem findings, illustrated by coloured micro-photographs of technical excellence. As might be expected from the whole sequence of events described in the clinical section, few organs of the body were unaffected. Chief attention is drawn to damage done to the heart and the brain.

Special studies (pp. 169–177) by W. H. LANGHAM with 8 named collaborators. These studies were made chiefly upon the urine, blood, and faeces during the life of the patient; subsequently most of the chief organs of the body were subjected to analysis. The chief object of all these tests was to compare the findings with those in previous cases in which there had been severe but not fatal radiation injury.

Dosimetric calculations (pp. 178–183) by P. S. HARRIS. The final results of measurement and calculation were as follows:— K's average total body exposure was probably between 3,900 and 4,900 rads, of which about 900 rads were due to fission neutrons; a considerably greater portion of the dose was delivered to the upper half of the body than to the lower half.

Health Physics Studies and Area Radiation Levels (pp. 184–187) by J. N. P. LAWRENCE with 4 named collaborators. The first indication of the accident outside its immediate vicinity was the activation of a criticality alarm in a building nearby. The workers there could find no source of trouble and *assumed* that the alarm had gone off accidentally. There are 8 continuous recording gamma monitors on site and 3 of them recorded the radiation burst up to 12,900 ft. away.

The whole record is one which many will want to read in detail. *S. Russ*

CEMBER, H., WATSON, J. A. & NOVAK, M. E. **The Influence of Radioactivity and Lung Burden on the Pulmonary Clearance Rate of Barium Sulfate.** *Amer. Indust. Hyg. Ass. J.* 1961, Feb., v. 22, No. 1, 27–32, 3 figs. [10 refs.]

There is evidence that pulmonary carcinoma is more likely to result from long-continued retention of inhaled radioactive dust than from more intense exposure in which the same total amount of energy is absorbed over a shorter period of time. Great differences in rates of clearance of dust from the lungs have been reported. The exact reasons for these differences are not well known, but they are thought to be influenced by factors such as the particle size distribution and the magnitude of the lung burden.

The effect of the lung burden on the rate of clearance of barium sulphate dust was studied in the experiments here reported. Parallel groups of rats were injected intratracheally with radioactive and non-radioactive barium sulphate particles which had a geometric mean particle size of 3·6 microns. There were 3 dose levels:— 23·3, 233 and 2,330 μgm.

The lung clearance with time was exponential. All doses had a clearance half-time of about 10 days, except the 2,330 μgm. radioactive dose, for which the half-time was 27·5 days. *Thomas Bedford*

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

PARRY, W. H. **The Survival of Salmonellae in Baked Confectionery.** *Med. Officer.* 1961, Apr. 7, v. 105, No. 14, 197–202. [32 refs.]

4 large scale baking tests into the survival of salmonellae in popular forms of confectionery made with naturally contaminated (Salmonella Thompson and Salm. Aberdeen) and artificially contaminated (Salm. Thompson or Salm. Senftenberg 775W) frozen liquid egg albumen were undertaken in Liverpool and by the British Baking Research Association.

The confectionery included angel slab cake, Genoese sheet, cup cakes, loaf cakes, meringues, lemon meringue pies, Japan biscuits and macaroons.

In the first test, with naturally contaminated material, salmonellae were isolated from 3 of 5 angel cakes, one portion of Genoese sheet and all 3 lemon meringue pies, prepared and examined in Liverpool. Cakes, with the exception of lemon meringue pies, prepared with albumen from the same tin, baked and examined by the BBRA were negative. The different results were said to be due to variations in baking times and temperatures, internal temperatures of cakes (203°F. for Liverpool, 212°F. for BBRA), number of samples examined, and methods used for examination.

The possibility of cross-contamination in the bakery was not excluded.

The second test was carried out in Liverpool with naturally contaminated albumen, one oven and a strict hygiene technique. 452 samples from similar baked products examined in Liverpool and by the BBRA were negative; 36 swabs taken from various sites within the bakery were also negative.

In the third test (Liverpool) with defrosted liquid egg artificially contaminated with Salm. Thompson, angel cakes were sterile, Salm. Aberdeen was isolated from 2 Japan biscuits and both Salm. Aberdeen and Salm. Thompson from one each of the macaroons; Salm. Thompson was isolated from several varieties of the meringues. 15 swabs from bakers' hands and equipment grew Salm. Thompson only. Salm. Aberdeen may have been present in the egg, or in the bakery after the first test, or the baker may have been an excreter.

In the fourth test liquid egg albumen artificially contaminated with Salm. Senftenberg 775W was used and a strict aseptic technique was observed by the BBRA but not by Liverpool. The organisms survived in one macaroon, one Japan biscuit and one meringue baked in Liverpool. Results obtained by the BBRA where the fully baked cakes were negative, indicated that Salm. Senftenberg survived for only 5 minutes, whereas in Liverpool the organisms were found in cakes after a 40-minute bake. 5 flies were found to be infected, and 8 swabs taken from baking equipment and the baker's hands were also positive in Liverpool; the positive findings might have been due to cross contamination.

It is concluded that normal baking of angel cake, Genoese sheet, loaf cakes, cup cakes and meringues destroys salmonellae in egg albumen, but that cross-contamination is a serious danger when egg products containing salmonellae are used in bakeries. Contamination may occur by contact with bakers' hands or bakery equipment previously contaminated by raw egg. Flies are also a hazard even when "splash" and soiling are reduced to a minimum.

[See also this *Bulletin,* 1958, v. 33, 153.]

Betty C. Hobbs

MURRAY, J. G. **The Incidence of Pathogenic Serotypes of *Escherichia coli* in Pasteurized Milk and Washed Bottles.** *J. Applied Bact.* 1960, Aug., v. 23, No. 2, 191–4. [10 refs.]

7,432 samples of pasteurized milk (high-temperature short-time method) from plant and distribution sources were examined by the presumptive coli-aerogenes and phosphatase tests in the period April to December 1959. Most samples were in pint or one-third pint bottles (school supply) but some were taken from churns of milk for hotels, hospitals, etc. 165 cultures were obtained which fermented lactose at 44°C. Agglutination tests showed that none of these strains of *Escherichia coli* was a pathogenic serotype.

From 1957 to 1959, 11,400 washed bottles were tested by the technique recommended by the Ministry of Agriculture and Fisheries (Technique No. B74·3 T.P.B. *The rinse method for the examination of washed milk bottles,* London: H.M.S.O.) 694 gave a positive result in MacConkey's broth at 30°C., but only 12 were positive at 44°C., and none of these was *E. coli* of a pathogenic serotype. The results confirmed the findings of previous workers that pasteurized milk does not appear to be a source of pathogenic serotypes of *E. coli.*

A small number of processing plants provided most of the 6·09% bottles giving a presumptive coli-aerogenes result at 30°C., presumed to be post-pasteurization contamination. The incidence of contamination was greatest with high atmospheric temperature.

All bottles giving a negative result in the presumptive test came from establishments where the management was good.

Betty C. Hobbs

AMERICAN J. CLIN. NUTRITION. 1961, May–June, v. 9, No. 3, 259–303. **Symposium on Additives and Residues in Human Foods.** [1] **Introduction** [LUCKEY, T. D.], 259. [2] **Additives and Residues in Foods of Animal Origin** [BIRD, H. R.], 260–68. [60 refs.] [3] **Chemical Residues and Additives in Foods of Plant Origin** [GOODMAN, R. N.], 269–76, 6 figs. [18 refs.] [4] **Industry Problems in developing Intentional Food Additives** [MAHONEY, J. F.], 277–82. [5] **Government Problems in dealing with Additives and Residues in Food** [DAY, P.], 283–7. [6] **Medical View of Additives and Residues in Foods** [COON, J. M.], 288–96. [15 refs.] [7] **Panel Discussion of Additives and Residues in Human Foods** [JACKSON, R. L. (Moderator); BIRD, H. R.; DAY, P. L.; MAHONEY, J. F.; COON, J. M.; GOODMAN, R. N.], 297–303.

FOOD POISONING

KRISKA, J., FERENCIK, M., KRCMÉRY, V. & LISKA, O. Experimentálne štúdie ichtyotoxikóz z údeného tunáka. I. Epidemiologické a chemické údaje. **[Experimental Study of Ichthyotoxicosis caused by Smoked Tuna]** *Československ. Hyg.* Prague. 1960, v. 5, No. 10, 580–85, 1 graph. [12 refs.] English summary.

50 of 148 patients in a hospital near Bratislava developed an illness characterized by hyperaemia of the face, macular erythema of the limbs and trunk, nausea, headache and fever, which came on 5–60 minutes after eating smoked tuna. The fish had been imported from Denmark in the frozen state, and had been left to thaw for 3 days before smoking. Investigation of the patients for the usual causes of food poisoning gave negative results, but an extract of the smoked tuna was highly toxic for guineapigs, which developed an asthmatic attack and died after 7–15 minutes. The fish was found to contain 40–320 mgm.% of histamine, which was evidently the cause of the poisoning. The patients recovered rapidly after anti-allergic treatment. *D. J. Bauer*

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

MCNALL, E. G., STERNBERG, T. H., NEWCOMER, V. D. & SORENSEN, L. J. **Chemical and Immunological Studies on Dermatophyte Cell Wall Polysaccharides.** *J. Investigative Dermat.* 1961, Feb., v. 36, No. 2, 155–7. [16 refs.]

Carbohydrate antigens were chemically extracted from strains of *Trichophyton mentagrophytes* and *Trichophyton rubrum* and the formulation of the former partially elucidated. It proved to consist of glucose and glucosamine in a ratio of approximately 2:1.

Chinchillas were immunized by injecting the *T. mentagrophytes* polysaccharide intramuscularly in a Freund adjuvant. Thereafter sera were obtained from the animals and subjected to precipitin tests with both the carbohydrate antigens.

Control animals contained no precipitating antibodies to either carbohydrate. Serum from the immunized animals gave positive precipitin reactions with both antigens but much more strongly with the antigen from *T. mentagrophytes*, *i.e.* the homologous antigen.

The authors state that these carbohydrate antigens are derived from the cell walls of the fungi but the process of extraction described does not seem to be as selective as that. They do not make it clear whether their control chinchillas received Freund adjuvant devoid of dermatophyte antigen or were totally uninjected. *Ian G. Murray*

MACKENZIE, D. W. R., BURROWS, D. & WALBY, A. L. ***Trichophyton sulphureum* in a Residential School.** *Brit. Med. J.* 1960, Oct. 8, 1055–8.

The authors describe their efforts to eradicate ringworm due to *Trichophyton sulphureum* in a residential school for girls.

Of 128 girls aged from 2 to 18 years, 20 were infected. They presented with various types of lesion: tinea capitis in 13; tinea corporis in 4; tinea capitis and corporis in 2 and tinea capitis and tinea unguium in 1.

Oral griseofulvin as administered to these patients in the dosage of 750 mgm. daily in divided doses (250 mgm. 3 times daily) over a period of 10 weeks. Topical treatment was also administered in the form of Bynamid ointment.

The effect of treatment varied according to the site involved; thus, lesions of the glabrous skin were clinically almost clear, usually within a month, except for a residium of infected follicle plugs; a finger nail appeared to be normal after 10 weeks, while scalp lesions tended to persist even after microscopy and culture had pronounced them clear. In the management of these lesions it was found beneficial to apply topical therapy to the scalp as well as oral therapy.

Prophylactic treatment with a single dose of 50 mgm. per day was administered to non-infected children; all fomites, including brushes, combs and bedclothes were disinfected as well as the flooring. *C. J. La Touche*

CRUICKSHANK, C. N. D., TROTTER, M. D. & WOOD, S. R. **Studies on Tricophytin Sensitivity.** *J. Investigative Dermat.* 1960, Oct., v. 35, No. 4, 219–23, 2 figs.

With the object of producing a purified trichophytin for testing purposes in order to make possible a more accurate assessment of human reactions to trichophytin, the authors carried out a series of sensitivity tests, first with guineapigs then with human beings.

Using an acetone-dried powdered mycelium of *Trichophyton mentagrophytes* they extracted it in various ways in order to determine which function

evoked the greatest reaction and in order to distinguish primary irritants from allergenic material.

An ethylene glycol extract was found to cause the greatest reaction in sensitized guineapigs and the smallest in control guineapigs, and was therefore used for the tests after undergoing various stages of purification which are described by the authors.

The reactions of sensitized guineapigs tested with these fractions are tabulated, and show that the purification stages eliminated reactions in the controls. There was however little difference in the intensity of the reactions to the different fractions.

Preliminary tests on human subjects showed that, of 15 persons who gave positive immediate reactions with commercial tricophytin 10 gave this type of reaction with the purified product; and of 11 giving positive delayed reactions with commercial trichophytin 8 gave this reaction with purified trichophytin. Finally, 8 reacted negatively to both preparations.

Guineapigs, whether inoculated initially with live or killed mycelium, when challenged a second time with living mycelium, produced earlier, more violent reactions than those which resulted from the initial infection or sensitization, and correspondingly, the reactions regressed within a shorter period than did those resulting from the initial infection or sensitization.

Immediate reactions to trichophytin were studied in both infected and sensitized guineapigs as well as delayed reactions, anaphylaxis, passive cutaneous anaphylaxis and passive transfer of delayed type sensitivity by peritoneal cells. *C. J. La Touche*

VANBREUSEGHEM, R. Traitement par la griséofulvine des onyxis dermatophytiques. [**Treatment of Fungal Infection of the Nails with Griseofulvin**] *Bruxelles-Méd.* 1960, June 5, v. 40, No. 23, 813–20. [10 refs.]

7 cases of skin and nail infection of the hands and feet due to *Trichophyton rubrum* in which oral griseofulvin was administered are described by the author in order to illustrate the vicissitudes and lack of uniformity in the results of treating such lesions with this drug.

The difficulty in obtaining complete cure of all infected nails is particularly stressed in contrast with the rapid and complete cures obtained in the case of glabrous lesions.

[See also this *Bulletin*, 1960, v. 35, 553.]

C. J. La Touche

BRUAUX, P. Traitement de quelques cas de teignes du cuir chevelu par griséofulvine. Note complémentaire. [**Treatment of Tinea of the Scalp with Griseofulvin**] *Ann. Soc. Belge de Méd. Trop.* 1960, Dec. 31, v. 40, No. 6, 873–8.

The English summary appended to the paper is as follows:—

"The results obtained by these various methods of Griseofulvin treatment are excellent. Actually among the 15 cases treated 11 were cured the cure being maintained for at least 1 month after the end of treatment (more than 2 months in 8). The total dose varied from 17–33 gm. and the length of treatment from 30–44 days. 1 case (No. 1) was also cured but it was not possible to keep it under observation for more than 3 weeks after the end of treatment. 2 cases of relapse 12 and 20 days respectively after the end of treatment were cured by a 2nd course (cure maintained for more than 1½ months after the end of the 2nd treatment). Finally 1 case (No. 4) was not cured after 42 days treatment but the drug was not taken regularly, and this case was not seen afterwards."

FRIEDMAN, Lorraine, DERBES, V. J. & TROMOVITCH, T. A. **Single Dose Therapy of Tinea Capitis.** *Arch. Dermat.* 1960, Sept., v. 82, No. 3, 415–18, 1 chart. [13 refs.]

Untreated prepubertal Negroid patients presenting with tinea capitis due to *Microsporum audouini* were subjected to a therapeutic trial in which the effect of a single dose of griseofulvin, 3 gm. in one day, was compared with the results from dosages of 1 gm. every 1, 2, 3, 5 or 7 days for 28 days, and 250 mgm. daily for 7 to 14 days followed by 3 gm. in one dose 32–39 days later. Controls were given placebos.

Results showed that, irrespective of the dosage schedule, most of the patients were clear of infection between the 6th and 8th weeks after initiation of treatment, and that some of them were clear before this time and others at a later date. There was no significant advantage to be gained from using a 3 gm. single dose schedule as against multiple 1 gm. doses administered at intervals of 2 or more days. *C. J. La Touche*

LOURIA, D. B., FALLON, Nancy & BROWNE, H. G. **The Influence of Cortisone on Experimental Fungus Infections in Mice.** *J. Clin. Investigation.* 1960, Sept., v. 39, No. 9, 1435–49, 12 figs. [30 refs.]

On the basis that the administration of corticosteroids enhances the severity of various kinds of infection including fungal infections, experiments were conducted to compare the effect of these drugs on experimental infections in mice due to *Histoplasma capsulatum*, *Cryptococcus neoformans* and *Candida albicans*, and when, after some preliminary work it was found that this effect was greatest in *Candida* infections, the problem of the pathogenesis of these infections was studied more closely and the effect of corticosteroids on them was analysed "when the infecting inoculum was small and when steroid treatment was delayed."

Results showed that the enhancing effects of cortisone on the course of infection with *Candida* was markedly diminished when cortisone administration was delayed. Thus, when it was administered before inoculation with 5×10^6 cells, 90% of the mice died. When it was administered the day after inoculation 70% died within 30 days, while postponement of administration of the drug for 1 week after inoculation reduced the mortality to 17·2%.

It was also shown that cortisone administration caused an increase in the renal census of *Candida* cells, even when the inoculum was about 10^3 cells, and that this

effect was greatest when cortisone was given 2 days before inoculation.

Histological investigations showed that infection was localized chiefly in the kidney in both control and treated mice, and it was thought that this was probably due to invasion of the tubular lumina by the fungus.

C. J. La Touche

TORRES BLASINI; Gladys, FIGUERAS, E. R. & SIFONTES, J. **Histoplasmosis in Puerto Rico.** *Bol. Asoc. Méd. de Puerto Rico.* 1960, Apr., v. 52, No. 4, 136–42, 1 fig.

Histoplasmin skin sensitivity tests carried out in 1957 on a group of 107 children under the age of 6 years who were in the Alejandro Ruiz Soler Sanatorium, and on 305 adults in the Cayey Sanatorium, showed that only 1 child gave a positive reaction, whereas, among the adults 35% gave positive reactions, most of which were intense.

Between December 1956 and June 1958, two of the authors also carried out a serological histoplasmosis case finding survey in Puerto Rico on subjects with "X-ray evidence of pleural pulmonary lesions or intrathoracic lymph node enlargement." The patients were aged from 18 to 81 years.

18% of 399 patients thus serologically tested gave positive results which, according to the authors, is a percentage comparable with that obtainable in endemic areas in the United States.

Animal inoculations and cultures were positive for *Histoplasma capsulatum* in only 1 case (an adult Negro aged 62 years) which is thought to be the first case of chronic pulmonary histoplasmosis on record for Puerto Rico. This case is described in detail.

C. J. La Touche

SASLAW, S., MAURICE, G. E., COLE, C. R. & CARLISLE, H. N. **Experimental Histoplasmosis in Large Domestic Animals.** *Proc. Soc. Exper. Biol. & Med.* 1960, Oct., v. 105, No. 1, 76–8. [15 refs.]

In pursuance of previous investigations on the pathogenesis of histoplasmosis in experimentally infected animals [this *Bulletin*, 1954, v. 29, 369; *ibid.*, 1960, v. 35, 654] the authors inoculated horses, cattle, sheep and pigs with *Histoplasma capsulatum*.

2 of each species and 1 of each sex were used in these investigations.

Inoculation was intrathecal with 5·0 ml. of a saline suspension of *H. capsulatum* yeast phase cells.

Results showed that all except the female sheep reacted clinically and serologically to infection with this organism. Fever persisting for at least 1 week occurred in 7 of the 8 animals at 3 to 5 days after inoculation. In the pigs, slight cough was exhibited, while definite symptoms of pulmonary infection were exhibited by the male sheep. Positive blood cultures were obtained from the male sheep and from the female pig.

After 75 days the female horse was rechallenged intrathecally, but exhibited no clinical signs of infection as a result. When, however, it was challenged again, this time intravenously, it exhibited obvious signs and symptoms of infection and died at 12 days after this further challenge. Histopathology revealed diffuse granulomatous pneumonia "superimposed upon foci with calcified centers and extensive peripheral fibrosis of more than 12 days standing." *H. capsulatum* was identified in the giant cells. It was thought that the tubercle-like lesions were caused by the previous intratracheal inoculation whereas the diffuse pneumonia process was brought about by the intravenous inoculation.

Evidence of lesions compatible with histoplasmosis were also noted in the autopsy material of both the sheep and the female pig, and, in the case of the male sheep *H. capsulatum* was observed in pulmonary lesions. No positive cultures of this organism were obtained from any of the experimental animals at autopsy.

The authors conclude from the results of these investigations that large domestic animals previously insensitive to skin tests with histoplasmin "can convert to skin test positivity after exposure to *H. capsulatum*".

C. J. La Touche

EDWARDS, Phyllis Q., AJELLO, L., MOORE, Jane, JACOBS, C. F. & ARONSON, D. L. **Soil Sampling in an Urban Focus of Histoplasmin Sensitivity.** *Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 747–51. [Refs. in footnotes.]

Experience has shown that *Histoplasma capsulatum* is found frequently in the soil of endemic areas, especially when this has been contaminated by the excreta of chickens, pigeons, other birds and bats [this *Bulletin*, 1959, v. 34, 224, 336; 1960, v. 35, 1188; 1961, v. 36, 36].

The authors were therefore impressed when they found a high rate of histoplasmin sensitivity in a section of the population of Dalton city, Georgia, in one area (A) which was relatively devoid of poultry [*ibid.*, 1959, v. 34, 763] and a lower rate in areas (B) where poultry were abundant. This discovery suggested to them the possibility of other, hitherto unknown, reservoirs of *H. capsulatum*.

Many possible soil sources in both areas which could provide soil reservoirs were sampled. These included residences and the grounds associated with them (all sites from which samples were taken being plotted on a map).

774 samples (reduced by pooling to make 64 for examination) were collected in April 1958, but none of these yielded any *H. capsulatum*. In September of the same year 528 samples were collected and of these only 1 sample yielded *H. capsulatum*.

The results obtained in these two successive surveys offer a further challenge to the authors to continue their investigations. *C. J. La Touche*

NICHOLAS, W. M., WIER, J. A., KUHN, L. R., CAMPBELL, Charlotte C., NOLTE, L. B. & HILL, Grace B. **Serologic Effects of Histoplasmin Skin Testing.** *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 276–9. [Refs. in footnotes.]

The authors remind us of the fact that repeated skin testing with histoplasmin in infected subjects may result

in raising the titres of complement-fixing and precipitating antibodies. They set out to determine the effect of a single skin test on complement-fixing antibodies.

2 groups of 50 and 63 patients, all being treated for tuberculosis, were chosen. The first group of 50 had all had previous skin tests with fungal antigens; they were bled immediately before, and at intervals after, a single skin test with commercial histoplasmin. The second group were bled immediately before and two weeks after a single histoplasmin skin test (and concurrent PPD and coccidioidin skin tests).

Both groups reacted similarly. Of the 113 patients, 42 gave positive histoplasmin skin tests, of whom 37 were serologically negative to *Histoplasma* antigens before the skin test (a titre of less than 1:8 being regarded as negative); 2 weeks or more later (for varying periods), 6 of these 37 gave titres of 1:8 to 1:16 in complement-fixation tests with histoplasmin, but remained negative where whole yeast phase *Histoplasma* antigen was used. Of the 5 who were originally positive to skin and complement-fixation tests, 3 remained serologically unchanged after skin test and 2 gave a reaction in a slightly higher titre (never over 1:32) on complement-fixation test with histoplasmin but not with whole yeast phase antigen. In the first group of 50 patients, a second skin test 3 weeks after the first did not affect the complement-fixing antibodies any further.

The conclusion reached is that the reliability of complement-fixation tests would be enhanced if blood for them was withdrawn either before, or within 1 week after, histoplasmin skin testing. *Ian G. Murray*

SALIBA, A. & BEATTY, O. A. **A Report of 12 Selected Cases of Pulmonary Histoplasmosis.** *Thorax.* 1960, Sept., v. 15, No. 3, 204–11, 6 figs. [12 refs.]

This report summarizes the clinical history of 12 cases of chronic histoplasmosis.

The clinical features and radiology of all these cases were not distinguishable from those found in cases of pulmonary tuberculosis, but laboratory investigations revealed the presence of *Histoplasma capsulatum* in sputum specimens or biopsies obtained from 11 of the patients, while "a highly positive complement-fixation" was obtained from the remaining patient despite negative cultures.

Amphotericin B, while found helpful in the treatment of these patients, did not bring about any dramatic improvement either clinically or radiographically.

It is concluded by the authors that the cultivation of a greater sense of "awareness of the prevalence of the condition and a closer scrutiny of bacteriologically negative 'tuberculous' cases may bring more cases to light." *C. J. La Touche*

FETTER, B. F. **Human Cutaneous Sporotrichosis due to Sporotrichum Schenckii; Technique for Demonstration of Organisms in Tissues.** *Arch. Pathology.* 1961, Apr., v. 71, No. 4, 416–19, 3 figs. [14 refs.]

The difficulty of demonstrating the causal organism of sporotrichosis in histological material is well known. The authors examined nine specimens of human tissue from which *Sporotrichum schenckii* had been cultured.

Straightforward Schiff-McManus staining gave poor results owing to the presence of a great deal of extraneous Schiff-positive material such as glycogen granules. However, it was found that if the Schiff-McManus staining was preceded by immersion of the section, after dewaxing and hydrating, in a 0·1% solution of malt diastase at 37°C. for 45 minutes, much of the interfering material was removed. At first saliva was used instead of malt diastase; this removed the glycogen granules but unfortunately deposited a number of organisms which could interfere with the diagnosis.

After the tissues had been so treated, 7 of the 9 showed round Schiff-positive bodies which were thought to represent the causal organism. In 8 of the tissues examined, the bodies were scanty, averaging one organism per 2 sections cut. In the 9th, from a Brazilian case, the organisms were very numerous and varied considerably morphologically. In no case was an asteroid body seen.

Although this procedure is a useful step forward in the demonstration of *S. schenckii* in human tissues it cannot be regarded as a substitute for cultural isolation in cases of human sporotrichosis. *Ian G. Murray*

KAPLAN, W. & IVENS, M. Sue. **Fluorescent Antibody Staining of *Sporotrichum schenckii* in Cultures and Clinical Materials.** *J. Investigative Dermat.* 1960, Sept., v. 35, No. 3, 151–9, 4 figs. [19 refs.]

The fluorescent antibody staining technique for the staining of pathogenic fungi has been gaining in popularity over recent years [see this *Bulletin*, 1958, v. 33, 947; 1959, v. 34, 1183; 1961, v. 36, 80, 349]. Accordingly, the authors decided to assess its value in the case of *Sporotrichum schenckii* both in direct preparations from pathological material and in culture.

Yeast-phase cells of *S. schenckii* were used as antigens, both in the live state and after being killed in formalin, for the production of antisera in rabbits which had been previously bled to provide normal serum which was to be used as the control against these antisera.

2 immune sera which had been obtained with live spore suspensions gave titres of 1:128, while 3 sera derived from rabbits immunized with formalin-killed cells gave a titre of 1:256, and 1 was anticomplementary. 5 of the normal sera were negative and 1 was anticomplementary.

Globulins were prepared by precipitation from the antisera and normal sera, and then combined with fluorescein isothiocyanate by a procedure which the authors describe in detail. The conjugated globulins so formed were then used for the staining of smears from cultures of *S. schenckii* and from purulent exudates in which the organism was present. Fixation of these smears was by heat.

This staining technique was applied to both the yeast and mycelial phases of *S. schenckii*, and, in addition, to a number of strains of other pathogenic fungi including: *Blastomyces dermatitidis*, *B. brasiliensis*, *H. capsulatum*, *H. duboisii*, various species of *Candida*, *Trichosporon* and others.

It was found that excellent results could be obtained with the diluted globulins derived from the antisera, particularly in regard to the cell-wall of the yeast phase. This fluorescent staining effect, which was yellowish-green, was exhibited also at varying intensities by the various elements of the mycelial phase when treated with these anti-serum globulins. In contrast, neither the yeast phase nor the mycelial phase exhibited this fluorescent staining effect when treated with normal serum globulins.

None of the heterologous organisms treated with conjugated globulins exhibited the type of staining seen in the various strains of *S. schenckii* so treated.

The authors conclude from their results that the fluorescent antibody staining technique as demonstrated by them is immunologically specific for *S. schenckii* and suggest its adoption as a diagnostic aid.

The appearances are illustrated in 4 figures.

C. J. La Touche

Brodie, J. & Henderson, A. **A Laboratory Study of the Candida spp. isolated in Aberdeen.** *Scottish Med. J.* Glasgow. 1961, Apr., v. 6, No. 4, 146–8. [21 refs.]

The authors correctly remind us that fungi with a yeast-like morphology cannot usually be identified as to species by microscopy alone. They examined yeasts from human sputum, throat and vagina to assess the relative frequency with which various *Candida* spp. occur. After recovery in pure culture, the *Candida* spp. were grown on dextrose and corn meal agars and fermentations were undertaken against glucose, maltose, sucrose and lactose. On these findings, classification was done according to the system of Martin *et al.* (*J. Bact.*, 1937, v. 34, 99). The average picture obtained from 500 sources was *C. albicans* 4·8%, *C. stellatoidea* 50·6%, *C. tropicalis* 19·6%, *C. parakrusei* 21%, *C. pseudotropicalis* 2% and *C. krusei* 2%. The disparity between their figures and those of other workers they attribute to the lumping together in the past of *C. albicans* and *C. stellatoidea* as a single species.

The grounds used by the authors for separating *C. albicans* from *C. stellatoidea* appear to be inadequate. The morphological differences described by Martin *et al.* are best noted on blood agar, which is not mentioned in this paper. Certain differentiation of *C. albicans* from *C. stellatoidea* can only be achieved by pathogenicity tests in rabbits and agglutination reactions with hyperimmune sera.

Ian G. Murray

Doupagne, P. Identification de 113 souches de *Candida*. Le Levine E.M.B.A., milieu idéal d'identification de *Candida albicans* en pays chaud. [**Value of Levine's EMB Medium for the Isolation of *Candida albicans* in Tropical Regions**] *Ann. Soc. Belge de Méd. Trop.* 1960, Dec. 31, v. 40, No. 6, 893–7.

The English summary appended to this paper is as follows:—

"A series of 113 strains of *Candida* have been isolated from pathological products in a tropical region. The strains were made up as follows: *C. albicans* 66%; *C. tropicalis* 22%; *C. guillermondei* 6%; *C. krusei* 2·6%; *C. parapsilosis* 2·6%. All save 1 were sensitive to mycostatin.

"All the isolated strains but especially *C. albicans* were cultured on Levine E.M.B.A. and Nickerson-Mankowski media. On the Levine medium, covering the area of sowing with a cover-slip hastened the identification of *C. albicans*. The use of Nickerson-Mankowski medium was difficult because of the ambient temperature (over 25°)."

Unat, E. K., Pars, B. & Kosyak, J. P. **A Case of Cryptococcosis of the Colon.** [Memoranda.] *Brit. Med. J.* 1960, Nov. 19, 1501–2, 4 figs. [11 refs.]

The clinical, pathological and mycological features of a case of cryptococcosis of the colon are described.

The patient concerned, a male student from Rize, Turkey, aged 16 years, gave a history, extending over several years, of intestinal disturbance which included persistent diarrhoea, bloody stools, tenesmus and abdominal pain.

On physical examination "a mass, the size of an egg, and slightly painful on pressure, in the left colic region" was discovered.

Surgery revealed a hard tumour-like mass adherent to the mesocolon, and situated in the descending colon. A resection was therefore carried out, after which end-to-end anastomosis was performed. The patient made an uneventful recovery.

The resected portion of the colon which measured 22 cm. long, showed, in addition to other abnormal features, "flat, nodular masses, 1·5 to 2 cm. thick, which on section showed soft pinkish and in certain parts myxomatous found foci, 0·5–1 cm. in diameter." Sections prepared from these myxomatous areas showed macrophages containing "one or, rarely, two round mycotic cells, the size of a lymphocyte." Some of these were surrounded by a clear transparent capsule which was well demonstrated in sections stained with mucicarmine. These structures were identified as a species of *Cryptococcus*. Positive cultures were not obtained.

C. J. La Touche

Smith, G. W., Kemp, J. A., Farrar, W. E., Jr., Kemble, J. W. & Philpot, D. F., Jr. **Cryptococcosis of the Central Nervous System: Four Cases treated with Amphotericin B.** *Southern Med. J.* 1960, Mar., v. 53, No. 3, 305–11, 3 figs. [15 refs.]

The clinical course of 4 patients suffering from cryptococcosis who were treated with amphotericin B is described.

The central nervous system was involved in all 4 patients, and *Cryptococcus neoformans* was demonstrated in each case either by culture or microscopically or both. The initial dose of intravenously administered amphotericin B varied from 12·5 mgm. daily to 50 mgm. daily. In 3 of the patients the maintenance dose was 50 mgm. daily, while in the other it was 35 mgm. every second day. In some of the patients more than one

course of amphotericin B therapy was administered. All the patients responded favourably to this treatment, and, when examined several months after they had been discharged, showed no tendency to relapse.

C. J. La Touche

BRAMLEY, P. & ORTON, H. S. **Cervico-Facial Actinomycosis. A Report on Eleven Cases.** *Brit. Dental J.* 1960, Sept. 20, v. 109, No. 6, 235–8, 5 figs.

These cases are collectively described in two groups, painless and painful.

(a) *Painless group.* 5 of the patients presented with "a slowly increasing, relatively painless, fluctuant swelling, with bluish overlying skin changes." This swelling was present at the identical site in all 5 patients, that is, "the crossing of the lower border of the mandible by the facial vessels."

The case described as representing this group concerned a youth aged 17 years whose molars were in an advanced stage of caries. When these were removed and tetracycline was administered recovery was uneventful. From this experience it is suggested by the authors that actinomycosis should be considered in the differential diagnosis of all swellings at the site of the crossing of the lower border of the mandible by the facial blood vessels.

(b) *Painful group.* The symptoms presented by 6 of the patients were "identical to those produced by an acute pyogenic infection of the soft tissues of the face and neck."

The abscesses in this group were at various sites, *e.g.*, in the submandibular area, at the angle of the mandible, in the parotid region, or in the neck. In both of the cases described from this group an acute abscess developed after extraction of a wisdom tooth. Extra-oral drainage and a 5-week course of tetracycline effected complete resolution in 1 case; in the other case no specific diagnosis was made and the abscess was drained. When however, it recurred, it was drained once more, and this time the organism was identified. The authors suggest that pus should be drained from the abcesses into a tube, not collected on a swab; since the "granules" are seen more distinctly in a tube. Differential diagnosis is with tuberculous adenitis, while the painful group is with acute pyogenic abscess.

Direct smears showed many branching filaments in all the cases, and *Actinomyces bovis* was grown in anaerobic culture from all the patients.

In conclusion the authors stress the importance of bacteriological investigations in such cases and recommend that tetracycline be the antibiotic of choice, to be administered in the dosage of 250 mgm. every 6 hours, with vitamin B complex, for 3–5 weeks, and accompanied by drainage.

C. J. La Touche

ALLAN, G. W. & ANDERSEN, Dorothy H. **Generalized Aspergillosis in an Infant 18 Days of Age.** *Pediatrics.* Springfield, Ill. 1960, Sept., v. 26, No. 3, Pt. 1, 432–40, 4 figs. [16 refs.]

Generalized aspergillosis has been rarely recorded in man.

The case reported in this article concerns a female infant aged 18 days. Abnormal signs and symptoms manifested themselves shortly after birth. Thus, on the second day of life a widespread macular rash developed, and from the third day of life, crying began which was accompanied by cyanosis.

There were no significant abnormal laboratory findings.

At 7 days the infant was discharged although there had been no alteration in her general condition. At home, the child's condition appeared satisfactory to the mother, except that she was not nursing well. At her 17th day of life she was medically examined and found to have an enlarged liver and to have failed to put on weight. A few crusted lesions were also present on the skin.

Chloramphenicol was administered, and topically, for the skin lesions, an antibiotic ointment. On the following day the baby died.

Autopsy revealed 5 crusted lesions on various parts of the body, including the scalp. The liver was enlarged; the pleural cavities contained no free fluid and the pleura was firmly adherent to the apices and diaphragmatic surfaces of the lungs; widespread granulomatous lesions were present in both lungs, the mediastinum, the diaphragm and in the liver, spleen and kidneys; small haemorrhagic erosions were present in the jejenum. The brain was not examined as permission to do so had been withheld.

Histological examination of the granulomatous lesions in the lung revealed central caseation with adjacent zones of necrosis. Thrombosed blood vessels were numerous in these lesions, as were also numerous branched septate hyphae. In the liver the lesions presented a somewhat similar picture. Hyphae were present also in the lesions of all the other affected viscera, including the thyroid gland and its artery.

Cultures from the liver, spleen and bowel yielded *Aspergillus fumigatus.*

This article concludes with a discussion regarding the possible source of the infection, which, it is thought, might have been intrauterine.

5 previously reported cases of generalized aspergillosis are tabulated [see, for example, this *Bulletin*, 1948, v. 23, 180].

C. J. La Touche

HOREJSÍ, M., ŠACH, J., TOMSÍKOVÁ, Alena & MECL, A., with the technical assistance of Dana BLAHNÍKOVÁ, Milada TUMOVÁ & Anežka VALISOVÁ. **A Syndrome Resembling Farmer's Lung in Workers inhaling Spores of *Aspergillus* and Penicillia Moulds.** *Thorax.* 1960, Sept., v. 15, No. 3, 212–17, 2 figs. [32 refs.]

This is a report of investigations into the causes of symptoms exhibited by a group of workers engaged in a citric acid fermentation plant in Czechoslovakia who were exposed to mould dust for a number of years.

Results showed a definite association between symptoms and exposure to mould dust over long periods. Confirmatory evidence of this was supplied by the results of culture, serological tests and sensitivity tests.

While, to some extent, the symptoms presented by the

patients resembled those of farmer's lung, the aetiology was, in the opinion of the authors, apparently different, in so far as organic dust derived from straw and hay is thought to give rise to the syndrome of farmer's lung whereas the patients in this series experienced their symptoms as a result of exposure to pure cultures of moulds.

There was moreover a high percentage (39·9%) suffering from chronic bronchitis among the younger group of workers, and a still higher percentage (70%) suffering from this disease among the older group of workers.

While there was no evidence to show that the moulds concerned (*Aspergillus niger*, *A. fumigatus* and various species of *Penicillium*) penetrated the bronchial mucous membrane or the lung parenchyma, their presence on the bronchial mucous membrane nevertheless provoked "repeated attacks of hyperaemia, hypersecretion, and spasm of the bronchi" which "are consequently followed by damage to the epithelium of the mucous membrane."

It was concluded also that, in one group of workers (group 2), despite the inhalation of the spores of both *Aspergillus* species and *Penicillium* species, the harmful effects observed were due to species of *Penicillium* rather than to species of *Aspergillus*. This was thought to be due to the weaker antibody response to *Penicillium* species as compared with that shown by the workers in Group 1.

Lastly, an interesting observation was the low occurence of streptococcal infections in both groups, a phenomenon which was thought to be due to antibiotic activity on the part of the moulds which were present.

C. J. La Touche

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

TUBERCULOSIS

CORBETT, J. T. **Tuberculosis amongst a Small Group of Indian Immigrants.** *J. College General Practitioners.* 1961, May, v. 4, No. 31, 332–7.

The author of this paper was responsible for the general medical care of a group of Indian immigrants in an English town. There were 22 persons, all from village communities in the State of Bombay, living in 3 houses. 6 of the 10 patients with tuberculosis were in house A, 2 in house B and 2 in house C.

The first patient was a woman aged 22 years who lived in house A. She was found to have renal tuberculosis and was admitted to the sanatorium in November 1957 and again in August 1959 with pleural effusion. In March 1958 her brother living in the same house had an ischiorectal abcess (presumed tuberculous), cervical adenitis and inactive pulmonary tuberculosis. Both patients received chemotherapy with good result. In April 1958 a man in house B was found to have tuberculous cervical adenitis and admitted to the sanatorium where he was treated successfully by chemotherapy.

The next 5 cases occurred between January and July 1959; the conditions found were sputum-positive pulmonary tuberculosis, pleural effusion, pulmonary tuberculosis, perianal abcess with minimal pulmonary tuberculosis, and pleural effusion. The first 4 of these patients lived in house A and the last in house B. The 1st patient mentioned was the only one found with a positive sputum; he lived in house A and may have been the original infector in the series.

The 9th and 10th cases occurred in house C. A woman was admitted to the sanatorium in October 1959 with tuberculous endometritis and salpingitis. In the same month her infant aged 4½ months was found to be a tuberculin reactor and to have cervical adenitis. His infection was thought to have been acquired congenitally from his mother. He was admitted to hospital for chemotherapy.

In November 1959 a wider survey of the Indian community was made in which 62 persons were X-rayed and no further cases of tuberculosis found. 30 males and 20 females were tuberculin-tested of whom 20 and 6 respectively reacted. All non-reactors were vaccinated with BCG. An infant aged 1½ years was found to react violently and to have an enlarged axillary gland; he was admitted to a chest hospital.

There was gross overcrowding in all the houses, and the diet was deficient. Moreover the English winter is severe for immigrants from the tropics, and in the community concerned, hard work in a dusty atmosphere caused frequent upper respiratory infections. With a better diet climatic conditions might be less important, and the author has little doubt that the most important factor in such an environment is overcrowding with consequent possibilities of cross-infection.

H. G. Calwell

LOTTE, A. & ROUILLON, A. Évolution de la tuberculose en France au cours des dix dernières années. **[Tuberculosis in France during the Last 10 Years]** *Bull. Inst. Nat. Hyg.* Paris. 1961, Jan.–Feb., v. 16, No. 1, 1–49, 36 figs.

In France the decline in mortality from tuberculosis, which started after the 1914–18 war, was interrupted by the outbreak of the Second World War and the death rate in 1941 reverted to the level of 1930 by rising to 158 per 100,000. Since 1941 the rate has fallen steadily to 23 in 1959 but this rate is much higher than the death rate in most European countries. The male death rate has been about twice that of the female and for both sexes the death rate now rises steadily through life; the pronounced peak that was present in young adult life, especially in the females, has disappeared. There has been little relative change in the regional or social class distribution of death rates from tuberculosis although there has been a large absolute fall in recent years.

Tuberculosis is not a notifiable disease in France and the trend of the incidence has been estimated from the returns of dispensaries and hospitals. The available data suggest that the fall in incidence has not been so rapid as the fall in mortality. This is in agreement with the trend in other European countries where large falls in the death rate have been accompanied by relatively small falls in incidence. *W. J. Martin*

LOTTA C. LA TUBERCOLOSI. 1960, Oct., v. 30, No. 10, 843–1071, numerous illustrations. [20 refs.] Convegno sulla epidemiologia della tubercolosi nel Lazio nel decennio 1948–1957, Rome, 15 June 1960. **[Conference on the Epidemiology of Tuberculosis in Lazio in 1948–1957]**

Modern Conception of Epidemiology (pp. 845–858), G. L'ELTORE.

This paper is of a general character. The term is now applied to the study of any disease, infectious or otherwise, which affects a community and calls for measures of control. We must investigate its origins, incidence, course, spread and decline and disappearance, in the present and also at other times and in other localities, with its distribution pattern by sex, age, social class and other relevant factors. Clinical studies must not omit any sub-clinical and symptomless incidence and any evidence of association with other diseases. Statistical data may suggest inferences which lend themselves to experimental checking. The control of epidemic illness is often dependent on very specialized biological investigations and the social study of the customs and environment of the affected community may prove of the utmost value.

Demographic, Social and Sanitary Situation of the Provinces of Lazio (pp. 859–941), O. CEINO, V. RUSTICHELLI, V. LAMMA, A. CERRUTI, V. DE SANCTIS, W. GALENO and P. VERDESCA-ZAIN.

The region is made up of the 5 provinces of Frosinone, Latina, Rieti, Rome and Viterbo. The area is 17,200 sq. km. and includes coast, plains, hills and mountains. There are some 3½ million inhabitants and the population density varies within a wide range, *e.g.*, 456 per sq. km. in Rome and 64 in Rieti. A considerable fraction of the territory is not suitable for agriculture and the region as a whole has fewer economic resources than many other parts of Italy. The topography and climate of the territory are discussed and numerous tables give information, often for each individual district, about resident population, housing, environmental and medical services, production, employment, income and expenditure, tuberculosis rates and mortality and other details, some of which are compared with corresponding data for Italy as a whole.

Estimation of Tuberculosis Infection in a Proportion of the School Population in the City of Rome (pp. 943–957), M. LUCCHESI, G. SPINA, D. ORICCHIO, G. PASTORE, and V. RUSTICHELLI.

The investigators carried out a tuberculin survey on 24,529 children, aged 14–16 years, from 88 representative schools: 62% were boys. The series included about 3 out of every 4 schoolchildren in that age-group. Dry anatuberculin of Petragnani on plaster was used by the Moro test, left on for 48 hours, and the result was read 24 hours later by a team made up of a school medical officer and 2 expert tuberculosis laboratory workers. 6,382 children, or 26%, were found tuberculin-positive. 3,558 of these and 12,487 of those found tuberculin-negative were X-rayed, and 12·8% of the former and 3·5% of the latter showed evidence of past primary lesions. 6 children, of whom one had been found tuberculin-negative, had active disease.

The authors consider that their findings reveal a high and efficient level of tuberculosis control. [Though the title of this paper refers to the "City" of Rome some of the schools were in the suburbs and in the nearby towns of Civitavecchia and Velletri.]

Ascertainment of Tuberculous Disease in Lazio (pp. 959–1041), O. CEINO and V. RUSTICHELLI.

Tuberculosis was diagnosed in 39,845 patients who attended the Lazio dispensaries during 1948–1957, and 17,351 of these dwelt in Rome. The case-rates work out at 1·19 per 1,000 for the whole of Lazio, 1·06 for Rome and 1·33 for the rest of the territory. These figures do not include such patients as those who privately seek advice from certain consultants in Rome, but this is not enough to account for the fact that the case rate for the city is only about half that in the rest of Rome province: the reverse picture is found in the other Lazio provinces. The authors refer to what L'ELTORE enunciated at the XIV International Congress in New Delhi (1957), namely, that when a community has passed through the endemic phase of tuberculosis the case-rate tends to drop under urban, while remaining still high under rural, conditions: they discuss the local factors in Lazio as these affect the rule which L'Eltore has formulated.

The paper includes numerous details for each separate district and each of the 10 years, such as new cases, sex and age distribution of incidence and mortality and so on. Men were more often affected than women in the approximate proportion of 3:2. The highest incidence was between the ages 5–24 years in Lazio as a whole, but more women were affected than men in the first 24 years of life; in Rome, this preponderance of

women patients persists to the age of 35. The highest mortality from tuberculosis has progressively shifted to the middle-aged and the old. More cases seemed to be diagnosed in the late spring. Occupational factors may have a causative significance; on the other hand a person may have chosen a static occupation, such as tailoring or hair-dressing, because the work appeared to be less strenuous. Primary forms had been diagnosed in 30% of the patients. Only 37% had had their sputum bacteriologically reported on, with a positive result recorded in 14%.

The authors review the treatment given, in and out of hospital, and the course of the disease. They discuss the drop in mortality and relate it to the introduction of antibiotic drugs; 1,090 died in the 10-year period. Among 20,596 cases which could be followed up, 2 out of every 3 patients approximately are known to have recovered.

[The authors report and comment on numerous other findings—too many to be dealt with in an abstract.]

Protective Measures against Tuberculosis in Lazio and Indications for their Application (pp. 1043–1071), V. Rusticelli, O. Ceino, A. Cerruti, V. De Sanctis, W. Galeno and P. Verdesca-Zain.

The authors refer to the local history of tuberculosis control from the beginning of the century. The law required the setting-up of provincial tuberculosis committees after 1927. They give an account of the present network of dispensaries and other tuberculosis institutions in the 5 Lazio provinces and they consider that only for Rome is the service entirely adequate. They emphasize the importance of the dispensary system for the early diagnosis and treatment of patients and for controlling spread of the disease. Tuberculosis in Lazio is in the endemic phase and tuberculin surveys aim at uncovering its scattered foci: a tuberculin-positive child points to the existence of an open case among its contacts, within or without the household. And when an open infection has been discovered in a person his or her contacts must be followed up and observed by periodical examination. Tuberculin-negative children among such contacts may become tuberculin-positive in a matter of weeks or months.

The control of tuberculosis is a community problem, is best organized by the authority and requires the cooperation of the public. Compulsory mass radiography should be considered for selected groups, *e.g.*, teachers and other school staff. When, as in Lazio, tuberculosis is in the endemic phase and the community has acquired a degree of resistance BCG vaccination offers fewer advantages than in the epidemic phases. In Rome, prophylactic isoniazid has been found useful for children under 15. Public assistance, health education, welfare and all other aspects of the tuberculosis problem need the fullest possible co-ordination.

J. Cauchi

Heycock, J. B. & Noble, T. C. **Four Cases of Syringe-Transmitted Tuberculosis.** *Tubercle.* 1961, Mar., v. 42, No. 1, 25–7.

4 infants who received intramuscular injections of penicillin at or about the same time were thereby infected with tubercle bacilli. A nurse who had given some of the injections to each of the infants was later found to have open pulmonary tuberculosis. No other source of the infection was found in the families or the environment of the children outside the hospital.

The first infant was aged 8 months on admission with pneumonia and enteritis in April 1957. He did not react to tuberculin. A course of intramuscular injection of penicillin was given. 3 months later he was admitted again with an abscess in the left buttock and was now a reactor. Tubercle bacilli were isolated from the abscess. The illness was prolonged and both antituberculous chemotherapy and surgical treatment were found to be necessary before healing took place.

The second infant aged 9 months was admitted at the same time with measles and pneumonia. He too was a non-reactor. Intramuscular penicillin was given, and 3 months later there was a swelling in the thigh, an abscess developed and tubercle bacilli were isolated from the pus. Tuberculin conversion had occurred. Specific chemotherapy was given but the tuberculous process went on to affect the right loin and the inguinal glands. Incision became necessary and chemotherapy was continued for 1 year.

The third infant was admitted with bronchiolitis 2 months before the first. Being only 6 weeks old he was not tuberculin tested. He was given intramuscular penicillin and at the age of 1 year had a deep abscess in the thigh from which pus containing tubercle bacill was evacuated. Specific chemotherapy was given. At the age of 17 months there were inguinal abscesses which discharged for 7 months before healing.

The last infant in the series was admitted at the age of 5 months with bronchiolitis in the same month as the first. The Mantoux test was negative. Intramuscular injections of penicillin were given, and 5 months after admission there was an abscess in the thigh. The Mantoux test was now positive. Specific chemotherapy was given and continued for a year.

At the age of 17 months the child had a respiratory infection which was again treated with penicillin during the continuance of the antituberculous chemotherapy. An inguinal gland abscess developed which was excised at 23 months.

By the age of 2¼ years the child was not yet walking, and 2 months later hydrocephalus was observed. There was acutely increased intracranial tension which led to death. The cerebrospinal fluid contained no cells. Necropsy showed massive internal hydrocephalus with thick fibrous adhesions which were regarded as probably due to earlier unrecognized tuberculous meningitis modified by chemotherapy.

This lamentable series of cases again emphasizes the need for routine X-ray examination of all medical and nursing staff and routine tuberculin testing of all children admitted to hospital. [See also this *Bulletin*, 1955, v. 30, 667, for a similar outbreak on a larger scale.]

H. G. Calwell

Morse, D. **Prehistoric Tuberculosis in America.** *Amer. Rev. Respiratory Dis.* 1961, Apr., v. 83, No. 4, 489–504, 7 figs. [Numerous refs.]

MOORE, M. E. **A Ten Years' Survey of Routine Ante-Natal Chest X-Rays.** *Tubercle.* 1961, Mar., v. 42, No. 1, 28–32. [14 refs.]

During the period 1950–59, 8,721 patients attending ante-natal clinics in Southampton were examined by X-ray. The work was done by mass miniature units. About one-third of the women attending ante-natal clinics in the city were X-rayed in the years with the highest numbers.

50 women were found to have abnormalities on the skiagram requiring further investigation at chest clinics; 1 was already attending a chest clinic and 5 were not fully investigated. The remaining 44 were found to have pulmonary tuberculosis.

34 of the patients were classified as having disease requiring treatment or close supervision, and 31 of these were given specific chemotherapy. 17 had not previously had X-ray examination and 22 had no pulmonary symptoms; 4 had positive sputa. All patients responded well to the treatment and have done well. 10 of the 44 patients were classified as needing occasional supervision; none of these had symptoms and only one was given specific chemotherapy.

The discovery rate of pulmonary tuberculosis either previously unknown or known was 5 per 1,000 examined; 3·9 per 1,000 required close supervision or treatment.

The cost of using large films was compared with that of small films and found to be £175 per 1,000 patients for large films and £11 per 1,000 for 70 mm. film. The author presents evidence that with modern equipment and technique it is possible to use miniature units without exposing the patient to an immoderate dose of ionizing radiation. He believes that mass radiography units could safely undertake the work of examining ante-natal patients—an important group as far as the discovery of tuberculosis is concerned. *H. G. Calwell*

SHENNAN, D. H. **A Modified Heaf Test using Old Tuberculin diluted One in Fifteen.** *Tubercle.* 1961, Mar., v. 42, No. 1, 33–9, 1 fig. [17 refs.]

It is a recommendation of WHO that the Mantoux test with 5 TU of PPD should be the standard test for the selection of candidates for BCG vaccination. Any more sensitive test could be regarded as excluding many people who would benefit by vaccination and would not be harmed by it.

The Heaf multiple puncture test has been found very suitable for mass BCG work but the opinion has been expressed that it is a very sensitive test which excludes too many suitable candidates. [The Heaf test with undiluted OT has been estimated as approximately equivalent to the Mantoux test with 30 TU.]

Shennan, working in Southern Rhodesia, made a trial of the Heaf test with various dilutions of OT to determine which is equivalent to the Mantoux test with 5 TU. African schoolchildren aged 6 to 18 years were tested. The dilutions of tuberculin used and the numbers tested with each were: 1/100, 116; 1/50, 217; 1/20, 148; 1/15, 621; 1/10, 384 and undiluted OT, 467. The Mantoux test with 5 TU of OT was done simultaneously as comparison.

It was found that all the dilutions used gave typical reactions of the same nature as those of the original Heaf test but the greater the dilution the fewer positive and strong reactions were found. It was concluded that a dilution of 1/15 with the Heaf test provides the nearest equivalent to the Mantoux test with 5 TU.

The Heaf test with 1/15 OT was then tried against the Mantoux test with 5 TU in 1,937 schoolchildren aged 6–18 years most of whom were being tested for the first time. 924 were tested with the Allen and Hanbury gun and 33·2% were found Heaf-positive and 32·7% Mantoux-positive. 1,013 were tested with the East gun and 19·0% were found to be Heaf-positive and 27·0% Mantoux-positive. [The discrepancy between the results with the two different guns is difficult to explain. Their pattern is different but mechanically their principle is exactly the same. Shennan does not say what depth of penetration he used.]

The conclusion reached is that the Heaf test with either gun using OT 1/15 or PPD, 0·13 mgm./ml. with the addition of 1 minim of 1/100 adrenaline per ml. is suitable for pre-BCG selection. [This criterion of selection would be more applicable to countries or areas where non-specific tuberculin sensitivity is common. The United Kingdom is not such and at present candidates for vaccination are selected by the Heaf test with OT or the Mantoux test with 10 TU of OT or PPD.]

H. G. Calwell

SILVER, C. P. **Hydrocortisone applied locally to Mantoux Reactions.** *Tubercle.* 1961, Mar., v. 42, No. 1, 40–42.

The author tested the efficacy of the local application of hydrocortisone to Mantoux reactions in reducing the intensity of erythema and induration [see also this *Bulletin*, 1959, v. 34, 875].

13 patients with active tuberculosis were the subjects of the 1st trial. They were tested simultaneously on both forearms by the intracutaneous injection of 10 TU of OT. After 24 hours the injection site on one arm was anointed with 1% hydrocortisone ointment and the site on the other arm with the ointment base only. Patients were allocated to either treatment at random.

At 24 hours, just before inunction, the average diameter of erythema on the treated side was 19·4 mm. and on the control side 18·3 mm. The average diameters of induration were 15·4 and 15·3 mm. respectively. At 48 hours the average diameter of erythema on the treated side was 26·1 mm. and on the untreated side 26·2 mm. The average diameters of induration were 18·2 mm. and 17·2 mm. respectively. Hydrocortisone thus applied was ineffective.

Mantoux tests with 1 TU were done on 11 patients with active tuberculosis. In this series 1% hydrocortisone ointment was applied 48 hours after testing, and 5 applications of hydrocortisone were made during the next 48 hours. The tests were read at 48 hours, just before inunction, and again at 72 and 96 hours. Again it was found that the hydrocortisone ointment was

ineffective. 2½% cream was used in a 2nd series of 22 patients with active tuberculosis. It had little effect in reducing the intensity of the Mantoux reactions.

In the final trial Mantoux tests were done on both arms in 10 subjects, 9 receiving 10 TU and one 1 TU. At 48 hours the average diameter of erythema was 27 mm. and of induration 18·6 mm. At 48 hours 7·5 mgm. of hydrocortisone sodium succinate was injected centrally into the Mantoux reaction sites of 4 patients and 5 mgm. into 6 patients. An equal volume of the vehicle alone was injected into the opposite Mantoux site as a control. In 5 subjects there was a considerable decrease in erythema, in 1 a moderate decrease and in 4 little or no change. There was no obvious change in induration. By the next day all the sites injected with hydrocortisone were indistinguishable from the control sites.

"The effect of hydrocortisone at this stage of the tuberculin reaction therefore appears to be on the blood vessels rather than on the cellular reaction."

H. G. Calwell

MAGNUSSON, M., BENTZON, M. W., BLEIKER, M. A., ENGBAEK, H. C., GRIEP, W. A. & MANTEN, A. **Comparative Intradermal Reactions of Tuberculosis Patients to Purified Tuberculin (PPD) and Purified Sensitin prepared from *Mycobacterium kansasii*.** *Acta Tuberculosea Scandinavica.* 1961, v. 40, No. 2, 85–102, 2 figs. [25 refs.]

Comparative intracutaneous tests were carried out on patients with tuberculosis in a sanatorium in Holland. The antigens used were PPD and "sensitin" prepared from *Mycobacterium kansasii* (photochromogenic acid-fast bacillus or "yellow" bacillus).

The object was to find out if the age of the patients and the duration of their disease had any effect on the size of the cross reactions and if such comparative testing could reveal sensitivity due to organisms other than *Mycobacterium tuberculosis* [this *Bulletin*, 1960, v. 35, 916].

36 female and 105 male patients completed the tests of whom 13 were Indonesian, 2 Chinese and the rest European. They were aged 17–82 years and none had been vaccinated with BCG.

The majority of the patients reacted to both antigens and gave larger reactions to PPD than to *kansasii* sensitin. There appeared to be a tendency to relatively larger reactions in patients who had been in hospital on one or more previous occasions with tuberculosis.

The distribution of reactions to PPD in both new and old patients was apparently normal with mean sizes of reaction of 15·6 and 15·4 mm. respectively. The distribution of reactions to *kansasii* sensitin was not normal in either group; in patients with long-standing disease it was bimodal. The mean sizes of reactions were 8·6 and 10·0 mm. respectively.

Sizes of reactions to both antigens decreased with the age of the patients, and the difference in reactions to them appeared to be less in patients over 60. This was significant only for the patients with new infections.

There were 10 patients whose reactions differed by less than 2 mm. These patients had a random age distribution. Such reactions occurred more frequently among patients with old than with new infections. There was no clinical reason for the unusual sensitivity of the 10 patients, and the only common finding was that 2 of them were brothers. Bacteriological and allergy studies of the organisms isolated from 5 of these patients revealed only 1 strain of *Myco. kansasii* while the others all seemed to be *Myco. tuberculosis.* The first mentioned strain evoked a pattern of sensitivity which was different from that invoked by the others all of which induced the same sensitivity as a strain of *Myco. tuberculosis.*

The animal study showed further that it cannot be concluded with certainty that a comparatively large reaction to a certain antigen indicates infection with the corresponding micro organism since animals infected with the strain of *Myco. kansasii* also showed increased sensitivity to avian tuberculin and Battey sensitin.

It was not clear whether the few relatively strong reactions to *kansasii* sensitin indicated previous non-tuberculous infection or a special response to infection with tubercle bacilli.

H. G. Calwell

RÖDIGER, E. Die Übertragbarkeit erworbener Tuberkulinnegativität auf Tuberkulinpositive. **[Transmission of Acquired Tuberculin-Negativity on to Tuberculin-Positive Adults]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1961, Feb., v. 121, No. 1, 12–31, 2 figs. & 1 diagram. [68 refs.]

Tuberculin sensitivity has been transferred passively to non-reactor animals by the intravenous or intraperitoneal inoculation of the cells of a sensitized animal or by the intracutaneous injection of a mixture of sensitized cells and tuberculin. Temporary sensitivity has also been produced in an infant by exchange transfusion with the blood of a reactor donor.

The object of the present experiment was to investigate the possibility of the transmission of acquired insensitivity to tuberculin to adult human reactors. PPD was used in the work in order to avoid the occurrence of the non-specific reactions which are likely with high doses of OT.

The subjects were adult women patients in a mental hospital. All were reactors at the outset and none had received antibiotic or other specific chemotherapy or cortisone or corticotrophin. They were given repeated doses of PPD in order to desensitize them; 5 dropped out of the experiment prematurely, only 2 became insensitive to 100 TU within 2 years, 2 reacted only to 100 TU at the end of 2 years, and 5 were still sensitive to 10 TU.

4 days after the last Mantoux test blood was taken from the 2 who were negative to 100 TU, from a woman who had reacted to 1 TU at the start and now reacted only to 100 TU, from a natural non-reactor to 100 TU and from a reactor to 1 TU. The sera were prepared and treated in various ways as detailed, *viz.*, with the addition of normal saline and tuberculin or saline alone.

In the rest of the experiment 3 groups of 20 mental

patients aged 40–82 years were used. None had previously been tested with tuberculin or had received specific antibiotic or chemotherapy or cortisone or corticotrophin.

The various sera were injected intracutaneously into 8 sites in each person and the reactions read at various intervals, recorded and analysed. It was found that within 72 hours after injection of a mixture of inhibitory serum and tuberculin into a reactor to 1 TU no reaction occurred in 8 out of 16 cases, in 5 cases the reaction was attenuated as compared with the control (1 TU) and in 3 cases there was no demonstrable inhibiting effect of the serum. However even in these 3 cases the reaction was markedly attenuated within 48 hours after the injection. It was seen that the inhibitory effect of the serum was even more marked after 48 hours than after 72 hours. Complete inhibition occurred after 48 hours in 12 persons, and marked attenuation of the reaction was seen in 4.

The findings are discussed and the author speculates on the existence of humoral desensitizing antibodies in tuberculin allergy. *H. G. Calwell*

McArdle, E. J. **A Survey of the Tuberculin Reaction of School Children in Kano Province: Northern Nigeria.** *West African Med. J.* 1961, Apr., v. 10, No. 2, 98–100.

Tuberculin surveys were made in 3 groups of schoolchildren in the northern region of Nigeria by using the Heaf test with PPD.

The 1st group comprised 1,170 Hausa children living in congested conditions in the city of Kano (population 130,000). Reactor rates rose from 25% at age 6 years to 81% at 13; the rates at 14, 15 and 16 were 78%, 85% and 79% respectively.

The 2nd group comprised 1,429 southern Nigerian children living in modern well-ventilated houses. Reactor rates rose from 16% at 6 to 60% at 13; the rates at 14, 15 and 16 were 59%, 51% and 68% respectively.

The 3rd group comprised 392 Hausa children from rural areas living in small villages or family compounds in surroundings which were much less congested than in Kano. The reactor rates rose from nil at 6 years (only 2 children tested) to 64% at 13; the rate in 19 children aged 14 was 42%.

The incidence of the various degrees of sensitivity found were:

	Group 1	Group 2	Group 3
Grade I (Heaf)	15	21·1	19·1
II	3·2	2·4	2·8
III	31	17·4	17·0
vesiculation	6·5	3·3	2·3

The high reactor rate in all groups indicates a high incidence of infection in the communities studied. [No mention is made of previous BCG vaccination of any of the children included. The high proportion with 1st degree reactions suggests sensitivity due to BCG or some other organism than *Mycobacterium tuberculosis*. Weak sensitivity of this kind is not characteristic of natural infection.] *H. G. Calwell*

Wagner, A. A. **Acute Miliary Tuberculosis of the Lungs in Africans.** *Central African J. of Med.* 1961, Jan., v. 7, No. 1, 15–16.

This paper reports the treatment of 18 patients with acute miliary tuberculosis during the past 5 years. These were uncomplicated cases. An additional case was complicated by tuberculous laryngitis, and one other with tuberculous meningitis was also treated. The patients were given 3 months daily treatment with 1 gm. of streptomycin, 300 mgm. of isoniazid, and 20 gm. of PAS. At the end of 3 months the PAS was discontinued. The patients were kept in hospital for 6 months, and streptomycin 1 gm. bi-weekly, and isoniazid 300 mgm. daily was continued. At the end of the 3 months treatment the chest X-rays had cleared completely and the patients were well. After a follow-up of 11–54 months this improvement continued, and there is no sign of deterioration. The patient with tuberculous laryngitis responded equally favourably. The patient whose case was complicated by meningitis made a good response but 7 months later he died from a recurrence of the meningitis. *F. H. Young*

Levy, D., Haapanen, J., Russell, W. F., Jr., Ninio, S., Nishio, K. & Middlebrook, G. **Studies on the Effect of Various Derivatives of Para-Aminosalicylic Acid on Serum Levels of Antimicrobially Active Isoniazid.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 4, 297–302.

The effect of various derivatives of PAS in combination with isoniazid is that it slows inactivation of microbiologically active isoniazid [this *Bulletin*, 1960, v. 35, 135]. The gastrointestinal intolerance of many patients for the free acid or its salts makes its use often difficult. This paper examines the question of how far the phenyl ester of para-aminosalicylic acid, and calcium benzamidosalicylate, can respectively, take the place of PAS in slowing the inactivation of the isoniazid.

25 adult patients were given 8 mgm. of isoniazid per kgm. of body weight twice daily without other drugs. On the morning of the test (the third day) a single dose of isoniazid, 8 mgm. per kgm. of body weight, was administered. Venous blood samples were taken before and 6 hours after the administration of this dose, and a second dose of isoniazid was then given. On the 4th day the patients received 8 mgm. of isoniazid per kgm. of body weight simultaneously with sodium para-aminosalicylate in a dose adjusted to contain 2·5 gm. of free PAS, and a second dose of sodium PAS was administered 3 hours later. Blood samples were then obtained for the microbiological determination of the serum level of active isoniazid.

On the seventh day these studies were repeated in the same sequence except that the patients received 8 mgm./kgm. isoniazid simultaneously with phenyl esters of PAS adjusted to contain 2·5 gm. free PAS, instead of the sodium PAS.

10 of the 25 patients had to be excluded as repeated experiments showed that the results obtained were not constant; in the other 15 constancy was obtained.

11 patients were then selected to compare the effect

of sodium PAS with that of calcium benzamidosalicylate adjusted to contain 2·5 gm. free PAS; 3 patients had to be excluded.

A significant increase of the active isoniazid was achieved by the administration of the phenyl ester of para-aminosalicylic acid, but this was somewhat less than was obtained by the sodium PAS. This was true for rapid isoniazid inactivators as well as the slow isoniazid inactivators. It was also found that the calcium benzamidosalicylate had a sparing effect on the isoniazid equivalent to that of the sodium PAS in those patients who were rapid inactivators of isoniazid. In the slow inactivators a somewhat lesser effect was obtained. [This is a very useful paper.] *F. H. Young*

STONE, H. & WIGLEY, R. D. **D-Cycloserine in Pulmonary Tuberculosis: a Trial of Low Dosage Cycloserine with I.N.H., including Previously Untreated Cases.** *New Zealand Med. J.* 1961, Jan., v. 60, No. 341, 23–4.

In this study cycloserine (500 mgm. in the case of women, and 750 mgm. in the case of men) daily, with isoniazid 300 mgm. daily, was used in 11 previously untreated cases of pulmonary tuberculosis. Sputum conversion occurred in 2 months in 10 patients, and 4 months in 1. Phenobarbitone was used to prevent neurotoxic effects, and in none were neurotoxic effects noted. 2 patients had transient skin rashes responding to antihistamines.

A comparative group of 11 patients was taken from the preceding period and treated with pairs of streptomycin, PAS or isoniazid in the dosage recommended by the Medical Research Council. The treatment with the cycloserine continued until the last patient in the control group had achieved sputum conversion. In view of the conversion of sputum it was impossible to determine as to whether isoniazid-resistant strains had emerged. 23 other patients were treated with cycloserine for various reasons, and in none of these did serious neurotoxic effects appear.

The authors suggest that cycloserine in small doses might be used instead of PAS where the latter is not tolerated. *F. H. Young*

CLARKE, G. B. M. & O'HEA, A. J. **Chronic Pulmonary Tuberculosis. Treatment with Ethionamide combined with Cycloserine or Oxytetracycline.** *Brit. Med. J.* 1961, Mar. 4, 636–8.

This paper reports the results of treatment with ethionamide either with cycloserine or oxytetracycline. The patients were all long-standing cases of pulmonary tuberculosis with a positive sputum and with organisms resistant to some, if not all, of the standard drugs.

12 patients received 250 mgm. of ethionamide 4 times daily, except for the first week when the dose was restricted to 250 mgm. twice daily. 5 of the 12 patients were given in addition 200 mgm. of cycloserine 4 times daily, and again the dose was restricted to 250 mgm. twice daily for the first week. The remaining 7 patients were given 250 mgm. of oxytetracycline 4 times daily instead of the cycloserine. 4 of the 5 patients in the cycloserine group achieved sputum conversion—based on an assessment after 6 months of treatment. In the other patient the organisms became resistant to ethionamide at the end of 9 weeks. In the oxytetracycline group 2 of the 7 patients achieved sputum conversion. A diminution in the number of tubercle bacilli seen in and isolated from their sputum was observed in 3 others.

In the cycloserine group cavity closure took place in 2 patients, and the cavities were smaller in 2 others of the 4 patients with cavities. In the oxytetracycline group the cavities were smaller in 5 patients with no change in 2. The main complication complained of was drowsiness. Contrary to expectation there was very little gastro-intestinal upset. 1 patient in the cycloserine group developed a unilateral gynaecomastia associated with ankle oedema. This disappeared after the withdrawal of the drugs. 1 patient in the oxytetracycline group developed jaundice in the 14th week.

Considering the type of patient the results were considered to be promising, but it was emphasized that this line of treatment is only really suitable for so-called salvage cases. *F. H. Young*

ARONOVITCH, M., GROSZMAN, M., BERKER, I. O. & HARLAND, W. A. **Some Clinical and Experimental Studies with Viomycin.** *Canadian Med. Ass. J.* 1961, Feb. 4, v. 84, No. 5, 263–7, 7 figs.

This paper reports on viomycin used on 38 patients with advanced tuberculosis who had become refractory to conventional chemotherapy. The average duration of treatment was close to 7 months; the dosage used was 2 gm. a day for 2 days a week given intramuscularly. The average amount of viomycin per patient amounted to about 120 gm. In only 3 patients was there sputum conversion and improvement in radiographic findings. In 7 there were severe enough reactions to require discontinuation of therapy. In view of the claim that viomycin pantothenate was superior to the sulphate these drugs were compared in a small number of patients. As far as could be determined the only advantage in the use of the viomycin pantothenate was that a greater number had their sputum converted to negative.

In view of the unsatisfactory results obtained it was decided to try the installation of viomycin into the bronchus by means of a plastic catheter introduced through the neck. No startling success resulted in the 4 patients in whom it was tried, but when the method was tried on rabbits it was found that an alveolar reaction occurred in the lungs, demonstrating that the material had reached the alveoli and had not been coughed up. *F. H. Young*

FROSTAD, S. **Can we rely upon the Fact that the Different PAS-Preparations really will be resorbed in the Gastro-Intestinal Tract after Oral Dosage? Some Observations during PAS Treatment in Pulmonary Tuberculosis.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 4, 303–7, 4 figs.

In the course of experiments undertaken for a different purpose it was found that in a female patient a

blood concentration of free PAS was obtained reaching 18 mgm. % in the first hour after an oral dosage of 15 gm. of granulated sodium-PAS, but after the same oral dosage of sodium-PAS in tablets there was a lower blood concentration, reaching 11 mgm. % in the first hour and increasing to 13 mgm.% after 5 further hours. The total PAS excreted in the urine was a little less with the tablets than with the granulated sodium-PAS. Experiments on other patients, however, did not produce the same findings except in patients with very constipated bowels.

A female volunteer who had a normal renal function and normal stools volunteered for a new experiment with a new series of blood and urine concentrations. 6 series of experiments were performed. High blood concentrations of the free PAS after oral medication of the granulated substance were obtained, and very low blood concentrations after the tablets. The same results were obtained in the urine. In view of this, on the evening before the date of a further examination the patient took carbo animalis enough to blacken her stools, and a further dose was prescribed 24 hours later. All the blackened stools were collected and examined for the presence of PAS. Not only were high concentrations of PAS found in the washing water, but also whole tablets, and fragments of tablets in the stools. The manufacturers of the tablets were informed and a new production set obtained. With these much better concentrations were obtained. Experiments showed that an additional complication to the use of PAS has been found, and it is now necessary to make certain that the tablets prescribed are in a condition which will allow the PAS to be absorbed satisfactorily from the gastro-intestinal tract.

F. H. Young

FAVEZ, G., TATTI, V., BOREL, C., VANNOTTI, A. & FREI, J. Effet d'une endotoxine, administrée pendant un mois, sur le cours de la tuberculose pulmonaire excavée momentanément rebelle aux antibacillaires. Contribution à l'emploi des oxynhyles (Reizstoffe). **[Effect of an Endotoxin Administered for a Month on Cavitating Pulmonary Tuberculosis Temporarily Refractory to Antibacterial Agents]** *Schweiz. med. Woch.* 1961, Feb. 11, v. 91, No. 6, 183–7, 4 figs. [13 refs.]

In an observation on 432 patients hospitalized for pulmonary tuberculosis and treated with antibacterial drugs it was found that in a certain number cavities were unchanged over a period although the bacilli were sensitive to the therapeutic agents used. This was noted in 29 patients. Patients born during an even year received intravenously a dose of an endotoxin extracted from *Salmonella abortus equi* on 6 days each week for one month after the cavity had been found radiologically stable for at least one month. In the patients born in an odd year the waiting period was 2 months or more. The antimicrobial treatment was of course continued. In the first group of 15 patients, the cavity closed itself during the non-specific therapy in 8 patients. Of the 12 who were allowed to wait for 2 months, cavities closed in 2 before the non-specific treatment was started. In 6 others the cavity closed during the non-specific therapy.

The authors consider that the condition of equilibrium between the bacilli and the host takes place in those types of patient in whom the cavities are stabilized, and that the use of the endotoxin, apparently lipopolysaccharide, breaks this impasse. [This is an interesting theory and experiment, but the results on larger groups of patients must be awaited.] [The substance is named Pyrexal, supplied by the Wander Laboratories; the dose was 0·5 μgm. rising by 0·5-1·0 μgm. daily to 6–10 μgm.] *F. H. Young*

MISRA, S. S. & KHANNA, B. K. **Corticosteroids in Tuberculous Meningitis.** *J. Indian Med. Ass.* 1961, Feb. 1, v. 36, No. 3, 89–92. [20 refs.]

This paper reports the results on 80 cases of tuberculous meningitis. 15 were treated by chemotherapy alone, 25 by chemotherapy with intrathecal streptomycin, and 40 with combined chemotherapy plus cortisone in the form of 20 mgm. of prednisolone per day orally in 4 divided doses. The results are shown below:

Showing the Final Results Obtained from Different Forms of Treatment

Treatment groups	Completely recovered	Partly recovered	Expired
Chemotherapy ...	7 (46·6%)	2 (13·4%)	6 (40%)
Intrathecal streptomycin ...	10 (40%)	4 (16%)	11 (44%)
Cortisone	28 (70%)	6 (15%)	6 (15%)

12% of patients treated with intrathecal streptomycin had cranial nerve paralysis at the time of their discharge from hospital, but otherwise the neurological sequelae were not very different with the various types of treatment. The average period of stay in hospital was definitely reduced from 58·6 days on chemotherapy to 34·6 days when cortisone was added. The follow-up study was not complete enough to be of statistical value.

F. H. Young

PRICHARD, R. W. & HAYES, D. M. **The Effects of Aminopterin on Guinea Pig Tuberculosis.** *Amer. J. Path.* 1961, Mar., v. 38, No. 3, 325–33, 6 figs. on pl. [15 refs.]

This study was originally undertaken to help in evaluating the significance of miliary tuberculosis found at the post-mortem examination of a child with acute leukaemia and who had been treated with aminopterin. The histological appearances of the tuberculous lesions suggested that the lesions post-dated the diagnosis of leukaemia, but there was the possibility that the aminopterin had interfered with the evolution of the tubercules.

Groups of 11 guineapigs were infected subcutaneously with H37Rv; one group received no treatment, and the others were treated with 2 μgm.

aminopterin per gm. daily, one from the day of infection, and the other from the day that they became tuberculin-positive. The tuberculin testing, with 1:1,000 OT, was done weekly, and all the surviving animals were killed after 42 days.

All the animals treated from the day of infection remained tuberculin-negative; 6 were dead by the 21st day and 3 more by the 35th day. Of the group to be treated with aminopterin when tuberculin-positive, 2 animals died on the 7th and 35th days before becoming positive and 4 more died during treatment. All the untreated animals became tuberculin-positive and 1 died on the 28th day and 2 on the 35th day.

Post-mortem examination of the untreated animals showed extensive tuberculous lesions with the usual histological changes; the examination of the animals treated with the antimetabolite from the day of infection showed a slightly smaller degree of gross organ involvement but with no caseation, in spite of the presence of many bacilli. The changes in the animals that were treated after becoming tuberculin-positive were midway between those of the other 2 groups.

In the discussion, the authors conclude that these results indicate that treatment with aminopterin can modify the morphological pattern of tuberculosis and that with large doses, caseation is abolished.

S. R. M. Bushby

WELTON, F. J. **The Compulsory Segregation of Uncooperative Tuberculosis Patients.** *Tubercle.* 1961, Mar., v. 42, No. 1, 91–4.

The Public Health Act of 1936 empowers local authorities in England and Wales to adopt a law compelling the isolation of uncooperative infectious patients with tuberculosis. Some authorities have taken this power and used it, some have taken the power and not used it and some have declined to have anything to do with compulsory measures.

A mass radiography survey made in Liverpool [population, 1951, 789,532] in 1959 discovered 162 new cases of infectious tuberculosis which shows that there is a considerable pool of infection in that city. During the period 1958–60 at least 8 patients were committed to hospital under magistrates' orders, and it has been the experience of the public health authority that the existence of the power to isolate, even if it is not exercised, is a valuable measure of persuasion.

The results of an enquiry made throughout Great Britain showed that medical officers of health generally favoured the use of compulsion in dealing with recalcitrant tuberculosis patients. Only 9 out of 115 stated that they objected to compulsion. Legal commital to hospital had been sought successfully in 14 places.

Welton emphasizes that compulsion is exercised for the protection of the community and not for the punishment of the patient. Every effort should therefore be made to gain his confidence and cooperation after he has been committed to hospital by the magistrate. With a declining incidence of tuberculosis and when hope of its eradication begins to be entertained the need for compulsory measures is likely to increase rather than decrease.

Compulsory power to isolate does not exist in Scotland or the area administered by the London County Council. 26 medical officers of health deplored this lack of power to deal with infectors. *H. G. Calwell*

PAUL, R. **The Effects of Vole Bacillus Vaccination of African Mine Workers in the Northern Rhodesian Copper Mines.** *Brit. J. Indust. Med.* 1961, Apr., v. 18, No. 2, 148–52.

Massive pulmonary fibrosis is accepted by many as being a modified form of pneumoconiosis due to the combined action of a low-grade infection and the specific dust causing the pneumoconiosis. There is therefore in some quarters doubt about the advisability of vaccinating workers with dust fibrosis against tuberculosis by the vole bacillus.

In the course of a vaccination programme in an African population the possible effect of the vole bacillus in accelerating massive fibrosis in African mine workers in Northern Rhodesia was studied. 17,697 mine workers took part and were tuberculin tested with PPD. 13,667 were found to be reactors and the 4,030 non-reactors were divided at random into groups of 1,984 who were vaccinated with vole bacillus vaccine and 2,046 who were left unvaccinated.

The tuberculin testing and vaccination were done in 1952–1956, and at the end of 1958 the radiological state of the 3 groups was analysed and compared with their state as recorded at the beginning. It was not possible to keep all the workers from each of the 3 mines under observation but it was not considered that this failure introduced an important bias into the investigation.

Details of the results of the X-ray examinations are given. The major radiological changes took place in the original reactor group. No person in either negative group developed massive fibrosis, and there were no accelerated radiological changes recorded in the vaccinated group. This was evidence that the vole bacillus had no adverse effect on pneumoconiosis. 3 persons in the negative unvaccinated group developed pulmonary tuberculosis. *H. G. Calwell*

VENEREAL DISEASES

WORLD HEALTH ORGANIZATION. **World Directory of Venereal-Disease Treatment Centres at Ports. Application of the International Agreement of Brussels, 1924, respecting Facilities to be given to Merchant Seamen for the Treatment of Venereal Diseases.** 2nd Edition. 164 pp. [Refs. in footnotes.] In French & English. 1961. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [8s. 6d.; $1.75; Sw.fr. 5.–.]

The introduction points out that the duties and functions of the Office International d'Hygiène publique were transferred to WHO in 1947 and this particularly applied to the Brussels Agreement of 1924 as regards venereal diseases; this included a list of treatment centres for venereal disease in ports throughout the world, a treatment booklet and an evaluation of the success of the scheme.

The text of the Brussels Agreement is set out in full in French, English and Spanish. This is followed by lists of countries which ratified the agreement and those which acceded to it ("accessions"); some countries made reservations and others implemented it informally. Technical definitions include venereal diseases, services, medical staff, technical equipment, hospital beds, medical care and supply of medicaments, in-patient treatment and Wassermann reaction.

Minimum requirements are set out in detail and include training of personnel, equipment in ports and equipment at sea; the personal booklet is described with examples of how it should be filled in together with code numbers to be used by the physician.

The remainder of this publication contains a list of treatment centres in ports in the various countries, which is useful for reference; this gives full details of their situation, times and days of opening.

In most cases treatment is free, but [surprisingly in the U.S.A.] in many places in-patient treatment has to be paid for. This book should be useful for reference, particularly to shipping companies and their medical officers who would do well to study carefully the "minimum requirements". *T. E. Osmond*

BROWN, W. J., SIMPSON, W. G. & PRICE, Eleanor V. **Reevaluation of Reactions to Penicillin in Venereal Disease Clinic Patients.** *Pub. Health Rep.* Wash. 1961, Mar., v. 76, No. 3, 189–98, 3 figs.

Reactions to penicillin occurring in 64 venereal disease clinics and 5 border reception centres in the United States over a period of 3 months in 1959 are analysed and compared with a similar series in 1954.

In 1959 total cases treated were 35,496 and reactions were 255 (7·18 per 1,000); or 9·71 for clinics only; the figure in 1954 comparable with this last was 5·95; the difference between these two is probably due mainly to more careful observation. It is noticeable that the incidence in 1959 was 9·71 for clinics and only 0·70 for reception centres; the explanation of this is probably that those treated at the latter were largely selected persons, young labourers and persons who could not be followed-up.

Of the reactions seen in clinics 146 were due to urticaria, 27 to anaphylaxis (9 moderate to severe), 11 to serum sickness, 25 to vertigo, 23 to pruritus, 14 to chills, etc. 18 to nausea, etc. and 19 to other various (only 1 case of Jarisch-Herxheimer reaction was seen). In general, the larger the total dose and the longer the duration of treatment the greater the number of reactions; sex made little difference but Negroes were much less susceptible than white persons; reactions also tended to increase with age but this is partly explained by the fact that the younger patients were usually treated for gonorrhoea with low doses, and the elder ones for syphilis with large doses. There was no difference between the two types of penicillin employed —procaine penicillin G in oil with aluminium monostearate and benzathine penicillin—nor was there any evidence that patients are becoming sensitized to penicillin, though patients who had previously shown reactions tended to do so again; however these usually reacted well to antihistamines.

It is concluded that no changes need be made in the current use of penicillin for the treatment of venereal disease, but emergency treatment should always be easily available. *T. E. Osmond*

NICOLI, J. & DEMÉ, J. Considérations sur le sérodiagnostic des tréponématoses en milieu africain. **[The Serodiagnosis of Treponematoses in Africans]** *Bull. Soc. Path. Exot.* 1960, Sept.–Oct., v. 53, No. 5, 848–62, 1 fig. [28 refs.]

This is a long and complicated study of the subject. The authors employed a number of tests, both lipoid and treponemal, in order to find out which indicated the presence of a treponematosis, syphilis or yaws, and which were probably falsely positive. The tests included among the lipoid the Kline, VDRL and Kolmer complement-fixation tests, and for the treponemal (TP) the Reiter complement-fixation test with antigen made by ultrasonic action and plain treponeme extraction; quantitative tests were also carried out. Results were classified as (1) both types positive, (2) both negative, (3) one positive and the other negative, (4) one doubtful and the other positive or negative. Sera from various sections of the population in Equatorial Africa were examined, including prenatal and routine specimens from rural dispensaries; different age-groups were separated. In one series of 155 persons both types were positive in 115 (75%), TP tests positive and lipoid doubtful in 21 (12%), TP positive only in 3 (2%) and lipoid positive only in 16 (10%).

As a result of a large number of tests it was concluded that treponemal tests were generally more specific than lipoid, that when both were positive a treponemal infection was almost certain, that if treatment caused a fall in titre this pointed strongly to a treponematosis, that presumed false positives were nearly always associated with low titres and that false positive reactions were relatively uncommon. It is recommended that as a matter of policy all sera should

first be tested by the Kline microagglutination test and that all those which are positive should be tested further by complement-fixation tests with cardiolipin and treponemal antigens. *T. E. Osmond*

MANDEL, E. H., MARKEL, J. & KIM, Y. P. **A False-Positive *Treponema pallidum* Complement Fixation (TPCF) Test. Report of a Patient with Herpes Zoster.** *J. Amer. Med. Ass.* 1961, Mar. 25, v. 175, No. 12, 1104–6. [10 refs.]

In the first part of this article the authors summarize the literature of false positive reactions in serum tests for syphilis (BFPR) quoting such extreme examples as "BFPRs account for 40 to 45% of the positive serological tests for syphilis" [this *Bulletin,* 1953 v. 28, 422], "BFPRs are reported in 100 per cent. of patients with malaria" and "an incidence of false-positive TPIs as high as 2·8 per cent".

Of the treponemal tests TPI is considered the most specific, followed closely by TPCF and RPCF (Reiter protein complement-fixation test.) A case is reported of a 30-year-old female suffering from chronic discoid lupus erythematosus and Weber-Christian disease. She had recently developed herpes zoster on the face and scalp. She gave the following reactions: May 1958 WR negative; Jan. 12, 1959 WR, Kahn, Mazzini, all positive; Jan. 19, 1959 Mazzini 4+, VDRL 2+, Kline exclusion 4+, Rein-Bossak 2+, cardiolipin CF 4+, TPCF positive and RPCF weakly positive; April 7, 1957 [? 1959] (1) WR negative, Kahn negative and Mazzini negative (2) Mazzini negative, VDRL negative, Kline exclusion negative, Rein-Bossak negative, cardiolipin CF negative, TPCF positive RPCF negative. Herpes zoster lesions had cleared by Feb. 11, 1959.

[TPCF has not yet been generally accepted as being 100% specific nor as being as specific as TPI; the fact that on 2 occasions TPCF was falsely positive in one laboratory throws some doubt either on the technique employed or on the specificity of the test].

T. E. Osmond

RANADE, S. N., KALYANPURKAR, S. S., DUBHASHI, A. R. & WABALE, S. M. **Sulphamethoxypyridazine in the Treatment of Venereal Diseases.** *J. Indian Med. Ass.* 1961, Mar. 16, v. 36, No. 6, 241–3. [19 refs.]

This drug is rapidly absorbed from the gastro-intestinal tract, is excreted very slowly in the urine, is highly soluble in urine and is only slightly acetylated in the body [this *Bulletin,* 1957 v. 32, 361.]

The authors treated 69 patients with the following results, gonorrhoea 30, cured 20, improved 7, failed 3: for chancroid the corresponding figures were 30, 22, 4, 4 and for lymphogranuloma venereum (LGV) 9, 9, 0. 0. The dosage was 2 gm. the first day followed by 1 gm. daily for up to 10 days for gonorrhoea and chancroid and up to 30 days (average 22) for LGV. There were no untoward side-reactions. The cure rate may well have been higher since some of the improved patients did not report for observation and may have been cured.

[These results are encouraging, but it may be that many strains of gonococci are less resistant to sulphonamides in India than in Europe.]

T. E. Osmond

FESTENSTEIN, H. & BOKKENHEUSER, V. **Attempted Induction of Immunological Tolerance in Rabbits using Living *Treponema pallidum*.** *Brit. J. Exper. Path.* 1961, Apr., v. 42, No. 2, 158–65. [21 refs.]

After a short review of the literature on immunological tolerance these authors describe how they infected with virulent *Treponema pallidum* 2 female rabbits 4 and 6 days respectively after mating; neither developed clinical syphilis but both produced reagin and immobilisin. None of the offspring showed any sign of syphilis serologically, histologically, microscopically or biologically up to 12–14 weeks. It is suggested that failure was due to the temperature of the mother's uterus being above the survival point of *T. pallidum.* [Surely this could be tested by inoculating the uterus of a female rabbit with living *T. pallidum.*] Thus it appears that neither *T. pallidum* nor its antigenic components can cross the placental barrier, and that congenital rabbit syphilis cannot occur. Other newborn rabbits were infected within 5 hours of birth and most died with 10 weeks though antibody formation proceeded normally; their tissues did not contain very large numbers of *T. pallidum.* Others treated with penicillin recovered and could later be infected experimentally.

Tolerance to *T. pallidum* was, therefore, not demonstrated. *T. E. Osmond*

POCHI, P. E. & STRAUSS, J. S. **The Single Dose Treatment of Acute Gonococcal Urethritis with Demethylchlortetracycline.** *Antibiotic Med.* New York. 1961, Feb., v. 8, No. 2, 75–7.

In an attempt to find a satisfactory drug which, in a single dose, would cure gonorrhoea these authors employed demethylchlortetracycline (7-chloro-6-demethyltetracycline) [this *Bulletin,* 1959, v. 34, 369]; they point out that a single dose is desirable because patients often cannot be trusted to take more than one and an alternative drug is needed in penicillin-sensitive patients.

43 male patients were treated with 0·9 gm. and 36 were followed up for 1 (14), 2 (15) or 3 (7) weeks by means of clinical examination, smears and cultures; 32 (89%) were cured and 4 (11%) were failures; of the latter, 3 showed disappearances of discharge but relapsed after 48 hours and 1 had prostatitis; all 4 were cured by penicillin. 6 patients (17%) showed side-effects which were mild in 3.

The success rate appears to be approximately the same as with other broad spectrum antibiotics given in single doses but somewhat lower than in those given large multiple doses. *T. E. Osmond*

WILLCOX, R. R. **Therapeutic Aspects of *Trichomonas vaginalis* Infections.** *Brit. J. Clin. Practice.* 1961, Mar., v. 15, No. 3, 233–9. [Numerous refs.]

The first part of this article is largely historical, recounting the various methods of treating these infections and their almost universal failure; only acetarsol has had any appreciable success in the past. Formerly treatment was entirely local but two drugs used systemically gave some promise—aminitrozole and trichomycin. This promise however was not fulfilled till the advent of metronidazole (8823 RP—"Flagyl").

The cases of 40 women treated with this drug (200 mgm. 3 times a day for 7 days) are reported; there was an immediate failure rate of 2 out of 34 followed (5·9%) and there were 7 relapses later; these are set out in detail in a table.

The causes of failure or recurrence are considered; immediate failure may be due to inadequate absorption or over-rapid excretion; recurrence may be true relapse or reinfection from an infected partner; in the latter case it seems that treatment of the partner should be carried out simultaneously whether he shows parasites or not.

[The cure rate does not appear as high as that reported by others [see this *Bulletin*, 1960, v. 35, 992; 1961, v. 36, 145 *ter*, 146 *quat.*]; perhaps the reason lies in the long observation period which extended up to 104 days.] *T. E. Osmond*

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

UNITED STATES DEPT. HEALTH, EDUCATION & WELFARE. **Infectious Diseases in the Aging. 1961 White House Conference Edition.** *Pub. Health Service Publication No. 762.* 1960. 238 pp., 10 figs. [Numerous refs.] Wash. 25, D.C.: Superintendent of Documents, U.S. Govt. Printing Office. [$1.50.]

This publication consists of a selection of articles and abstracts published in the last 2 decades: it is planned in 5 chapters. Each chapter, except the third, consists of several articles by different authors, followed by a series of abstracts and a list of selected reading. The titles of the 5 chapters are *General, Respiratory, Skin and Special Sensory Organs, Cardiovascular and Gastrointestinal.*

In the first article *Infectious Diseases in Old Age, Their Incidence, Clinical Characteristics and Therapy* (pp. 3–30) F. D. ZEMAN points out that whereas in youth the body's reactive processes are at their height and the virulence of the organism is the dominant factor in an infection, in old age the defence processes are so modified that organisms of low virulence may lead to serious disease. Arterial changes may affect the function of tissues and organs throughout the body, particularly those concerned with response to infection. Cardiac reserve may be depleted by infection and failure precipitated: resulting pulmonary oedema provides a culture medium for bacteria. Diabetes is a well-known hazard, and nutritional problems, especially concerning proteins and vitamins, are closely related to general resistance and to the occurrence of bedsores and skin sepsis. Gallstones or prostatic hypertrophy are followed frequently by infection of the biliary or renal tracts.

The symptomatology of infection in the aged is often deceiving. Pneumonia and peritonitis may reach an advanced stage with no pyrexia and almost complete clinical latency: cardiac infarction may supervene during a mild infection. Infection may produce symptoms of psychosis so acute that the real cause of the condition is missed. In the gall-bladder and the appendix the lymphoid tissue may be so atrophied by the ageing process that gangrene, rupture and widespread peritonitis may occur with almost no clinical evidence of the acute inflammatory stage. Neoplasm may be masked by infection. In spite of the many difficulties, the problem of infection in the aged can be tackled intelligently and hopefully, and Zeman's article, from the Home for Aged and Infirm Hebrews, New York City, is obviously based on wide clinical experience.

In *Problems of Chemotherapy in the Older Age Group* (pp. 41–52) D. LEHR from the Departments of Medicine and Pharmacology, New York Medical College, considers the problems of sensitization, nephrotoxicity and bacterial resistance. It has been estimated that 100 to 200 anaphylactoid reactions to penicillin occur annually in America with 30% mortality and an increasing number are in the older age-groups. Because of renal and arterial disease, nephrotoxic reactions to drugs are a hazard in the aged: triple sulphonamide mixtures and the broad spectrum antibiotics are relatively safe but streptomycin, neomycin, bacitracin and polymixin B are all specially liable to cause nephrotoxic damage. Sulphonamides are much less likely than the antibiotics to lead to superinfections with resistant organisms and they should be used in preference to them whenever possible. In chronic broncho-pulmonary infections combined penicillin-sulphonamide therapy is more successful and less dangerous than wide-spectrum antibiotics, and in urinary infections sulphonamides should always be the drugs of choice, antibiotics being reserved for infections proved to be resistant to sulphonamides. Chemotherapy in the aged is not essentially different from that at any other age but greater care is required in the selection and administration of the drugs.

In the section on respiratory diseases, H.

Rosenwasser deals with infections of nasal sinuses and the ears (pp. 67–73): in institutions for the aged he recommends early treatment and isolation of patients suffering from the common cold or other minor respiratory infections. P. S. Rhoads in *Pneumonia in the Aged* (pp. 75–82) stresses the rarity of primary pneumonia with classical clinical features in the aged: pneumonia usually develops insidiously on an underlying pathological basis with some degree of respiratory obstruction—*e.g.* emphysema, bronchiectasis, hypertension—and complications arise not so much from the infective agent as from these underlying causes. L. M. Barber, Clare N. Rees and L. Mazzadi in *Tuberculosis—A Geriatric Problem* (pp. 83–87) stress the need for more beds for patients in the 60 to 80 age-group.

The chapter on *Skin and Special Sensory Organs* consists of abstracts only, relating mainly to the care of the ageing skin. In the chapter on cardiovascular conditions, H. Kjörstad in *Rheumatic Fever in the Aged* (pp. 109–121) refers to a shift towards the older age-groups in patients treated in hospital for rheumatic fever. He describes the symptomatology of the disease in 46 patients over 50 years of age: the course of the disease may be protracted with very little fever, moderate joint symptoms and a low incidence of cardiac damage: the response to salicylates is excellent. F. D. Zeman in *Subacute Bacterial Endocarditis in the Aged* (pp. 123–146) reviews the literature to show that the incidence of the disease in the aged is not insignificant: he gives details of 18 patients ranging from 60 to 87 years. One-half of the patients had a typical, though often modified, clinical picture: in the others the disease was masked by a variety of other clinical findings, especially involving the central nervous system. The essential thing is to be aware of the possibility of this disease occurring at advanced ages as modern therapy can be successful irrespective of age. R. G. Petersdorf and R. K. Merchant in *A Study of Antibiotic Prophylaxis in Patients with Acute Heart Failure* (pp. 147–156) found that the administration of 2 gm. chloramphenicol daily for 7 days to patients in acute heart failure did not prevent the onset of pneumonia. It is better to search for pulmonary infection, by clinical and radiological methods, and to treat it early with appropriate drugs.

In the chapter on gastro-intestinal infections, M. M. Reeves, D. Meredith and F. J. Lewis, in *Appendicitis in the Older Patient* (pp. 165–167) show that the mortality in their series was 9·9% in patients over 45 compared with 0·2% in patients under 45. Delay in seeking medical advice and the rapid spread of the infection in the older person are the most obvious causes. G. Alsted in *Studies on Malignant Hepatitis* (pp. 169–179) reports on a very malignant form of hepatitis prevalent in Denmark since 1944: it occurs predominantly in women over 45, runs a protracted course and has a mortality of 50%. H. D. Bennet in *Hepatitis in the Geriatric Patient* (pp. 181–187) found little difference in the course and prognosis of infective hepatitis in the aged but serum hepatitis was commoner in the older group and caused a mortality of 25% in those over 60 compared with 7·1% in younger patients.

Mary D. Pettit, Catherine B. Hess and Jane M. Leibfried in *Geriatric Gynaecology* (pp. 199–209) discuss the examination of the ageing patient and the various abnormalities that may be encountered. This article, a valuable review of its subject, seems out of place in this symposium as it deals almost entirely with structural defects and neoplastic changes rather than infections. In *Pyelonephritis—Its Natural History and Course* (pp. 211–235), C. S. Keefer reviews the causes and incidence of acute and chronic pyelonephritis at all ages with special emphasis on the condition in the aged when it is usually found associated with obstruction of the lower urinary tract. When due to single strains of organisms, the acute infection can usually be cured by the use of the appropriate anti-infective drug. Further basic information is required about "the biological behaviour of bacteria in the kidney, how they arrive there, why they are so difficult to eliminate and why reinfection is so common."

This symposium brings together much valuable information about the problem of infection in the aged. It makes a plea for persistent investigation of infections in the aged and for an intelligent and hopeful application of modern therapeutic agents. *A. B. Christie*

Levine, L., Ipsen, J., Jr. & McComb, J. A. **Adult Immunization. Preparation and Evaluation of Combined Fluid Tetanus and Diphtheria Toxoids for Adult Use.** *Amer. J. Hyg.* 1961, Jan., v. 73, No. 1, 20–35, 1 fig. [14 refs.]

For 7 years the Massachusetts Public Health Biologic Laboratories have been producing a combined fluid tetanus and diphtheria toxoid vaccine intended primarily for reinforcement of immunity in adults without previous Schick or Moloney testing. A dose (0·5 ml.) contains 1 Lf unit of diphtheria toxoid and 5 Lf units of tetanus toxoid. The fluid preparation is preferred because (a) it was found that it is as effective (for adult reinforcing immunization) as the corresponding alum-precipitated preparation (which has so often been proved superior in animal assays), and (b) it was felt that it would probably cause fewer and smaller reactions. The use of a vaccine with such a low (but minimum effective) content of toxoid raised the problem of stability: this was overcome by adding 0·35% human serum albumin, using isotonic phosphate buffered saline, and reducing the merthiolate [thiomersal] content to 1 in 30,000. The content of diphtheria toxoid is too low to pass the official test for fluid diphtheria toxoid, and special tests (based on comparison with a reference standard preparation) had to be developed to check the flocculating level and the antigenic potency of the diphtheria component. Field studies, the results of some of which have already been published, have been conducted throughout the 7 years and the massed results are analysed to show the efficacy of the vaccine. 1 Lf of diphtheria toxoid is shown to be a satisfactory reinforcing dose (even 0·2 Lf invoked a response not significantly smaller than that due to 1 Lf). Although 1 Lf tetanus toxoid produces an appreciable amount of antitoxin, 5 Lf gives a better response without any evidence of a significant increase in the number or degree of reactions. Interesting figures are given of reactions to

the vaccine: practically all of them can be ascribed to the tetanus toxoid. 20% of subjects had some kind of reaction and 10% had reactions of greater than local significance. The incidence of reactions rises markedly after the age of 25 years, and the number of repeated reinforcing immunizations is less important than is the fact of having received basic immunization. As well as in field studies the combined vaccine has been used in many large-scale clinics throughout Massachusetts and the overall experience has been favourable.

D. A. Cannon

HOSPITAL AND OTHER CROSS INFECTIONS

WILSON, Miriam G., NELSON, R. C., PHILLIPS, Laura H. & BOAK, Ruth A. **New Source of *Pseudomonas aeruginosa* in a Nursery.** *J. Amer. Med. Ass.* 1961, Apr. 1, v. 175, No. 13, 1146–8, 2 figs. [18 refs.]

"During routine bacteriological culturing of fomites within a nursery, *Pseudomonos aeruginosa* was found in sinks and faucet aerators. Water from these faucets was used to wash hands and to clean equipment and may have contributed to the difficulty encountered in eliminating Pseudomonas from cleaned incubators. Hands washed within the room with the contaminated water could easily have transmitted Pseudomonas to the susceptible premature infant.

"The recent concern for the increasing numbers of Pseudomonas infections emphasizes the necessity of recognizing and removing within a hospital all wet, stagnant environments conducive to the growth of this organism.

"*Pseudomonas aeruginosa* was found again in the sink outlets several months later. The joints and fittings under the outlets were grossly dirty, and Pseudomonas was invariably obtained from these locations. Repeated cultures of the water showed no Pseudomonas growth. The outlet of the sink is routinely cleaned last."

COCCAL INFECTIONS

The order in this section is:—***Staphylococcus, Streptococcus, Neisseria, Others.***

WISSLER, H. Die Staphylokokkenpneumonie des Kindes. **[Staphylococcal Pneumonia in the Child]** *Schweiz. med. Woch.* 1961, Apr. 1 & 8, v. 91, Nos. 13 & 14, 385–9; 416–19, 7 figs. [40 refs.]

This is an excellent account and review of the features of staphylococcal pneumonia in the child. There are descriptions of its prevalence, age distribution, pathogenesis, clinical picture and the findings on X-ray examination. A number of detailed case histories are given with an account of the diagnosis, prognosis and therapy. In a section on the epidemiology of the disease there is a discussion of the staphylococcal carrier state with mention of the value of phage-typing of isolated strains and also emphasis on outbreaks of the infection in hospitals particularly in lying-in institutions.

In summary staphylococcal pneumonia occurs mainly in the first 2 years of life and is very often severe and deaths occurring in 24–48 hours are not uncommon. The case mortality is high and is 20% in the Children's Hospital in Zürich. The X-ray findings are not pathognomonic but abscess formation is frequent followed by empyema or pyopneumothorax. Peribronchial abscesses may cause pneumatoceles which are very characteristic. The treatment of choice is by large doses of broad spectrum antibiotics. *M. E. Delafield*

NARASIMHAN, P. **The Use of Intrathecal Enzyme Pancreatic Desoxyribonuclease along with Systemic Antibiotics in the Treatment of a Severe Staphylococcal Meningitis.** *Indian J. Med. Sci.* 1960, Sept., v. 14, No. 9, 780–84, 2 figs. on pl.

SAKUMA, T. **A Comparison *in vitro* of some Anti-staphylococcal Antibiotics.** *Yokohama Med. Bull.* 1960, Oct., v. 11, No. 5, 341–51, 13 figs. [20 refs.]

The author writes from Yokohama, but has recently been working in Houston, Texas, and his subject is a strain of *Staphylococcus pyogenes* from the blood of a 27-year-old man treated in a hospital at Houston for septicaemia caused by intravenous narcotic self-administration. This infection did not respond to penicillin, streptomycin, chloramphenicol or kanamycin but was cured with vancomycin. The results of conventional tests of bacteriostatic and bactericidal action against this organism of these and other antibiotics are first reported. Further tests with only 3 of them by an extremely elaborate method are then described. They consisted of inoculating broth containing 5 different concentrations of the antibiotic with an inoculum of 4 different magnitudes (10^8, 10^7, 10^5 and 10^3 organisms per ml.) and performing viable counts after 3, 6, 12 and 24 hours. The results are presented graphically. The action of erythromycin was predominantly bacteriostatic: kanamycin was fairly rapidly bactericidal, but with some tendency (referred to in the text but not evident in the graphs) for organisms to "multiply after being partly killed". Vancomycin exerted the most effective bactericidal action, particularly on the largest inoculum, and it is suggested that such a test with such an inoculum may be a valuable guide to the treatment of a severe infection. *L. P. Garrod*

CORNFELD, D., HUBBARD, J. P., HARRIS, T. N. & WEAVER, Ruth. **Epidemiologic Studies of Streptococcal Infection in School Children.** *Amer. J. Pub. Health.* 1961, Feb., v. 51, No. 2, 242–9, 1 fig.

Throat cultures were taken from children [apparently about 1,000 in number] in 3 schools in Philadelphia

once a month, and at the time of any respiratory tract illness, for 3 years, and in 1 school for a 4th year. In 1 school penicillin was given to all children yielding haemolytic streptococci on culture and to their contacts; this school consistently had a lower carrier rate for haemolytic streptococci than the others. In a 2nd school, where penicillin was given only if there were respiratory tract symptoms as well as a positive culture the carrier rates were similar to those in a 3rd, control, school. In all 3 schools about 50% of the children had at least 1 positive culture each year; and there was no difference in the incidence of respiratory illnesses associated with positive culture. Persistent carriers were fewer in the school given the most penicillin treatment. No clinical difference could be detected between illnesses associated with streptococcal infection and those not so associated nor were there particular bacteriological features. Antistreptolysin increases were more common in children with positive cultures than in those with negative cultures. The results of this survey are thought to contra-indicate community control programmes for streptococcal infection based on the administration of penicillin to all children found to be infected with streptococci. [For earlier parts of this study see this *Bulletin*, 1959, v. 34, 443, *bis*.]

R. E. O. Williams

Cornfeld, D. & Hubbard, J. P. **A Four-Year Study of the Occurrence of Beta-Hemolytic Streptococci in 64 School Children.** *New England J. of Med.* 1961, Feb. 2, v. 264, No. 5, 211–15, 3 figs. [18 refs.]

This paper records an analysis of the streptococcal experience of 64 children attending a school in Philadelphia through 4 years; the investigation covers part of a larger study [see Cornfeld *et al.* above] of which the children seemed to be representative.

Monthly throat cultures yielded carrier rates ranging, in different years, between 6·4 and 17·5%; in 3 of the 4 years the rate rose in the Spring. There were a total of 212 acquisitions of new strains of streptococci during the 4 years; 55 of these were associated with illness. There was only 1 case of reinfection with a single type and that was in a child treated with penicillin for the first illness. The antistreptolysin titre of the children's serum was found to be correlated with the number of times on which they had been carriers during the previous year, varying from about 30 in those newer carriers to about 100 in those who had had 3 or 4 periods of carriage. There was no correlation between the titre and the subsequent carrier experience.

R. E. O. Williams

Stillerman, M. & Bernstein, S. H. **Streptococcal Pharyngitis. Evaluation of Clinical Syndromes in Diagnosis.** *Amer. J. Dis. Children.* 1961, Apr., v. 101, No. 4, 476–89, 8 figs. (1 coloured on pl.). [15 refs.]

This is an attempt, from a study of 1,141 cases of acute pharyngitis, to correlate clinical with bacteriological findings. Of 228 cases diagnosed as streptococcal on clinical grounds, 78% showed streptococci on culture. A scarlatiniform rash and petechiae on the soft palate were regarded as the two most dependable, though also the most infrequent, signs: marked redness or oedema of the oropharynx, exudate on tonsils or pharynx and enlarged tender anterior cervical lymph nodes were more frequent though less specific signs. [There is considerable, rather laborious, analysis of symptoms, signs and bacteriological findings: the conclusion seems to be that an experienced clinician can make a fairly shrewd bacteriological diagnosis on clinical grounds.] *A. B. Christie*

Kevy, S. V. & Lowe, Betty A. **Streptococcal Pneumonia and Empyema in Childhood.** *New England J. of Med.* 1961, Apr. 13, v. 264, No. 15, 738–43, 7 figs. [16 refs.]

Of 93 children treated for pneumonia in the Children's Hospital Medical Centre, Boston, U.S.A., between June 1958 and June 1959, 11 were found to be suffering from pneumonia due to haemolytic streptococci. Case reports of 3 children are given: the first illustrates the resemblance of haemolytic streptococcal to virus pneumonia, the second describes the development of streptococcal empyema in a patient being treated with tetracycline and the third records the occurrence of gangrenous and purpuric lesions on the extremities of a patient suffering from streptococcal pneumonia. Penicillin is superior to broad-spectrum antibiotics in the treatment of these cases. *A. B. Christie*

Breese, B. B., Disney, F. A. & Talpey, W. B. **Triacetyloleandomycin—a Substitute for Penicillin G. A Comparison of the Therapeutic Effectiveness of Triacetyloleandomycin, Erythromycin Propionate, and Oral Penicillin G in the Treatment of Beta Hemolytic Streptococcal Infections.** *Amer. J. Dis. Children.* 1961, Apr., v. 101, No. 4, 423–8, 1 fig. [12 refs.]

The authors treated 3 groups of 87, 93, and 95 children suffering from streptococcal infection with erythromycin propionate, potassium penicillin G, and triacetyloleandomycin: the drug was given by mouth in each case for 10 days. All 3 drugs rapidly controlled the disease initially but recurrences were more frequent with erythromycin than with penicillin or triacetyloleandomycin. When follow-up observations were limited to 1 month, penicillin and triacetyloleandomycin were equally effective but when longer periods were considered the carrier rate was higher with penicillin than with triacetyloleandomycin. The authors feel that penicillin is still the best drug for streptococcal infections, having regard among other things to cost, but that in patients allergic to penicillin triacetyloleandomycin is a satisfactory alternative. *A. B. Christie*

FEINSTEIN, A. R.; SPAGNUOLO, M.; GILL, F. A. **The Rebound Phenomenon in Acute Rheumatic Fever. I. Incidence and Significance** [FEINSTEIN, SPAGNUOLO & GILL]. *Yale J. Biol. & Med.* 1961, Feb., v. 33, No. 4, 259–78, 3 figs. [22 refs.] **II. Treatment and Prevention** [SPAGNUOLO & FEINSTEIN]. *Ibid.*, 279–98, 6 figs. [25 refs.]

I A study of 265 children and adolescents showed that the rebound phenomenon consisted of 2 types—the "laboratory" type in which there was an increase in the values of the erythrocyte sedimentation rate or serum C-reactive protein, and the "clinical" type in which there was recurrence of symptoms. The "laboratory" type was of no permanent significance and did not cause cardiac damage. The "clinical" type was characterized by recurrence of joint pains and fever; in 10 of 49 patients further cardiac damage occurred in patients who initially had valvular involvement. The rebound phenomenon did not occur in patients not given anti-inflammatory treatment, and was commonest in those given steroid therapy. The authors think that the rebound phenomenon is due to the suppression of rheumatic inflammation by drugs and that this inflammation reappears when the suppressive drug is reduced or stopped.

II Treatment is not required for laboratory rebounds nor for clinical rebounds in patients with no initial cardiac damage. In patients with valvular involvement but no cardiac enlargement new cardiac murmurs may appear but these do not necessarily signify new valvulitis and they tend to disappear whether treated or not. In patients with initial cardiac enlargement, a rebound may produce severe new cardiac damage. These patients must be given anti-inflammatory treatment although its cessation will probably be followed by another rebound. No type of therapy seems to prevent these secondary rebounds but combined salicylate-steroid therapy may reduce the incidence of primary rebounds.

A. B. Christie

FEINSTEIN, A. R. & SPAGNUOLO, M. **The Duration of Activity in Acute Rheumatic Fever.** *J. Amer. Med. Ass.* 1961, Apr. 1, v. 175, No. 13, 1117–19.

Activity in rheumatic fever persists until the acute clinical and laboratory abnormalities cease and anti-inflammatory treatment is withdrawn. The authors studied this period in 265 patients and found that the mean duration in days for patients with valvular involvement was 124 and for patients with undamaged hearts 89. In patients who had a short course of anti-inflammatory therapy and then had a clinical rebound which was not so treated, the total duration of activity was almost identical with that found in patients whose entire attack had been untreated. This suggested to the authors that the total duration of rheumatic activity in a patient remains unaltered by treatment, so long as the original course of treatment is shorter than the natural course of the acute inflammation.

A. B. Christie

BROWNELL, Katharine D., LOSTY, Margaret A. & O'SHAUGHNESSEY, Helen M. **A Community Plan by an Official and Voluntary Agency for Patients with Rheumatic Fever.** *Amer. J. Pub. Health.* 1961, Feb., v. 51, No. 2, 250–55.

The plan described in this paper began as a joint effort of the New York City Health Department and the New York Heart Association in one district of Manhattan. In 1952, it began to expand to the rest of Manhattan. It was then called the "Manhattan Cardiac Program." Its objectives were case finding, verification of diagnosis and education of practising physicians. When the prevention of development of heart disease became a possibility by the use of prophylactic drugs the Health Department and the Heart Association provided them for the indigent. There is now a "Joint Committee on Prophylaxis" containing representatives of the Heart Association, the City Health Department, the Visiting Nurse Service and the clinics themselves for general oversight of the scheme. There are now 74 clinics with formal prevention programmes with some 4,000 patients receiving prophylaxis. They are 76% of those rheumatic children whose names are on the Manhattan register. Also, the City Health Department operates 2 special clinics itself. They provide diagnostic and follow-up services as well as prophylactic drugs. Case finding is largely through the school health service. In the adult clinics the Visiting Nurse Service is helpful in getting patients to attend regularly. Clinic difficulties arise because of the frequency with which the patients change their addresses and when a child, because of age, has to transfer to an adult clinic. There is, as yet, no central register for the whole city. Another difficulty is that almost 40% of the children in Manhattan are Puerto Ricans whose parents speak little English. The prophylactics used are oral penicillin and sulphadiazine. A conference has recently been convened of all the people concerned, including the hospital clinicians, to evaluate the work already done and to make proposals for the future.

Allen Daley

SPINELLI, N. P. R., BROWN, H. A. & LAVNIKEVICH, N. J. **Operation of a Cooperative State-Wide Rheumatic Fever Prevention Program.** *Amer. J. Pub. Health.* 1961, Feb., v. 51, No. 2, 256–60.

This is a brief history of the Connecticut State programme for preventing recurrences of rheumatic fever in known rheumatic subjects by prophylactic drugs. It began in 1954 by informing practising doctors of the scientific value of the method. The drug chosen was buffered penicillin G to be given by tablet in a dose of 250,000 units daily.

As a result of negotiation with the drug houses the cost was one dollar a month per patient. The scheme was sponsored by the Connecticut Heart and the Connecticut Pharmaceutical Associations and endorsed by the State Medical Society and the State Department of Health. The State Department of Health paid for the cost of the drug when the patients could not afford even the reduced price. A doctor desiring the penicillin

for one of his patients sends particulars to the Heart Association who file them and send to the doctor a pad of prescription forms to last a year.

By June 1959, 5,927 applications had been received from 1,061 doctors. A majority of the patients were adult: 33% were in the age-group 25–44 of whom 65% were women. A check is kept of the prescriptions issued but not dispensed. Failure to obtain the drug reaches substantial proportions. The 42% who had not obtained it for over a year were dropped from the programme. Steps are being taken to obtain the services of a public health nurse for follow-up work. Recurrences are reported by the doctors to the Heart Association and the number has been surprisingly low.

Allen Daley

DEAN, C. **Administrative Phases of a Rheumatic Fever Prophylaxis Program on a State-Wide Basis.** *Amer. J. Pub. Health.* 1961, Feb., v. 51, No. 2, 261–5.

The programme described in this paper started in 1943 with a pilot scheme in 7 rural and sparsely populated counties of Michigan. It was sponsored by the Michigan Crippled Children Commission and aided financially by the Federal Children's Bureau. In January 1956 it was extended to the whole State. It is based mainly on monthly intramuscular injections of benzathine penicillin G given in the surgeries of family doctors. The doctors can refer patients for diagnosis to hospital out-patients' departments staffed by specialists. A register is maintained by the State of all known rheumatic patients. The procedure for follow-up and for removal from the register is described.

An analysis of the figures for the first half of 1959 showed that 371 children were receiving benzathine penicillin G and 22 sulphadiazine. In addition, 50 had dropped out: 10 had ceased to attend: 10 had moved and could not be traced: 9 had changed to drugs not included in the programme: in another 9 their doctors advised that the drug be discontinued: 3 reached the age of 21 which is the age limit for the programme: 3 married, 1 died and there were various reasons for discontinuance in the other 5. In cases where the family is impoverished a small fee is paid to the doctor for giving the injection and the monthly examination.

The essentials for success are close cooperation between the State Health Department and the State Crippled Children Commission: good diagnostic and consultative centres and an educational scheme for doctors and parents.

Allen Daley

SHAFFER, J. D. & THOMPSON, W. B. **A Coordinated Approach to Prevention of Rheumatic Fever.** *Southern Med. J.* 1961, Jan., v. 54, No. 1, 65–70, 1 fig. [10 refs.]

An ambitious scheme of prevention of rheumatic fever is outlined. It involved the active cooperation of the State Health Department, school authorities, visiting nurses' associations, bacteriological laboratory, and private physicians in finding cases of early haemolytic streptococcal infection, and in securing treatment for them adequate for the elimination of the organisms. The scheme was applied to 567 schoolchildren aged 6–10 years in Oklahoma City. During the winter of 1958–59 there were in this group 305 individual absences due to upper respiratory infections, as ascertained by the school secretary telephoning or otherwise communicating with the parents. A visiting nurse then took a throat swab and recorded the temperature, and this was done after an average period of illness of 1–6 days. Approximately half the cultures grew *Streptococcus pyogenes.* The 4 significant clinical features were sore throat, fever, pain on swallowing, and swollen tender cervical glands. The private physician was informed by telephone of the 173 illnesses with positive cultures, and invited to give adequate treatment (for 10 days) as recommended by the American Heart Association. Nevertheless 47 of the children actually received inadequate therapy, and there were also 47 children found to be still positive in follow-up cultures. The latter were sent home and arrangements made for further therapy until their cultures were clear.

No case of rheumatic fever developed in the group, although the expected number was said to be 5 or 6. The procedure is stated to be applicable to entire school populations *if one can orient and educate the population to the values of prevention in medicine.*

H. Stanley Banks

BACTERIAL INFECTIONS

The order in this section is:—***General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.***

SEMPLE, A. B., PARRY, W. H. & PHILLIPS, D. E. **Diphtheria in Liverpool.** *Lancet.* 1961, Apr. 29, 937–8.

This is a report of 2 outbreaks of diphtheria in Liverpool during 1960: in the first there were 1 case and 1 carrier, in the second 2 cases and 2 carriers: one of the children in the second outbreak died. In both outbreaks the infection seemed to have been imported from abroad. In the first there were only 11 contacts and these were given combined active-passive immunization. In the second there were many more contacts and 24,205 children were given primary or booster doses of antigen.

A. B. Christie

DONALDSON, P. & WHITAKER, Jo Anne. **Diagnosis of Pertussis by Fluorescent Antibody Staining of Nasopharyngeal Smears.** *Amer. J. Dis. Children.* Chicago. 1960, Apr., v. 99, No. 4, 423–7, 1 fig. [10 refs.]

Nasopharyngeal smears were taken from 67 paediatric patients with a clinical diagnosis of whooping-cough, from 36 control subjects and from 13 healthy siblings exposed to infection, over a period of 6 months at the

Departments of Microbiology and Pediatrics, University of Texas Southwestern Medical School, U.S.A.

Rabbit antisera with titres of over 1:500 against *Bordetella pertussis* were conjugated with fluorescein isothiocyanate, adsorbed with ion exchange resin and diluted 1:10 to increase specificity and brilliance of staining. Smears were stained together with positive and negative controls and examined appropriately. A positive result was recorded if more than 3 typically stained bacteria were observed after 5 minutes search over 50 microscopic fields.

The control group was entirely negative. Of 36 untreated patients with clinical whooping-cough 31 gave positive smears. In 2 of the 5 negative cases the subsequent clinical courses left the diagnosis equivocal.

Of the 31 patients treated with antibiotics 13 were on therapy for less than 48 hours and all gave positive smears although 9 showed only minimal numbers of organisms. In the 18 patients on therapy over 48 hours only 2 positive results were recorded.

Examination of smears from 13 healthy siblings exposed to infection revealed *B. pertussis* to be present in 2 cases without subsequent development of clinical whooping-cough. Positive smears were also obtained from 2 apparently healthy control subjects who later developed the disease and were not tabulated. These are considered to have been in the catarrhal stage when the specimens were taken.

In the few cases where culture for *B. pertussis* was undertaken smears made from the early and mixed confluent growth stained specifically with labelled antibody.

Advantages of this technique over the more usual cultural methods are simplicity, rapidity, specificity and high sensitivity where even non-viable organisms can be recognized. The sensitivity of immunofluorescence for diagnosis in the catarrhal stage remains to be investigated while the present study suggests this technique should enable reliable clinical and epidemiological data to be obtained. *John Gordon*

BERG, J. M. Complications neurologiques de la coqueluche. [**Neurological Complications of Whooping Cough**] *World Neurology*. Minneapolis. 1961, Jan., v. 2, No. 1, 56–65. [30 refs.]

This is a discussion, based on the literature, of the neurological complications of whooping-cough. Reported incidence varies from 15% to 0·8% but depends on what is regarded as a neurological complication—some authors omit convulsions. Convulsions may be focal or generalized and may be followed by coma lasting for hours, days or weeks. Neuritis, radiculitis, myelitis and other non-cerebral complications have been described. Physical sequelae, commonly epilepsy or spastic paralysis, are not uncommon: long-term mental sequelae are more difficult to estimate. Mortality has been reported as between 30% and 80%—again it largely depends on what type of complication is included in the totals. Treatment is unsatisfactory. *A. B. Christie*

BREIJER, H. B. G. & WOLFF, H. L. **Incidence and Diagnosis of Intestinal Infections on Board Sea-Going Vessels.** *Trop. & Geograph. Med.* Amsterdam. 1960, Dec., v. 12, No. 4, 315–26. [19 refs.]

The main interest of this paper is the method of investigating intestinal disturbances among passengers and crew of a ship at sea. Samples of faeces were collected on filter paper, dried and then forwarded by air mail from the next port of call to an appropriate bacteriological laboratory for examination. About 350 faecal specimens were examined by this method and in 41 instances shigellae or salmonellae were isolated by the bacteriologist. Apart from one or two small outbreaks of dysentery, probably introduced into the ship by shore visits at a port of call, most of the cases of gastro-enteritis or dysentery appeared to be of a sporadic nature. There were no explosive outbreaks. The ships concerned were both passenger and cargo vessels belonging to the Rotterdam Lloyd Line on journeys to and from the East and in most cases the dried faecal specimens were sent from the nearest port of call directly by air mail to the University Laboratory of Tropical Hygiene in Leyden. *H. J. Bensted*

PUSCHMANN, B. Über den klinischen Verlauf einer Salmonella Thompson Hausepidemie. [**An Epidemic of Salmonella Thompson Infection in a Children's Clinic**] *Ztschr. f. ärztl. Fortbildung.* 1961, Mar. 15, v. 55, No. 6, 297–301, 1 fig.

In the period June 1959 to February 1960 an epidemic of salmonella infection occurred in a children's clinic. There were 52 cases of Salmonella Thompson and 1 each of Salm. Derby and Salm. Heidelberg infection. The epidemic had 2 phases—in June to November there were 35 cases in infants, and in December 1959 to February 1960, 19 infants and young children were affected.

The epidemic had a sudden onset, with the explosive illness of several infants at the suckling stage. The symptoms and signs, fully described, were mainly vomiting with green, watery, slimy stools; a high temperature and rapid loss of weight of as much as 400 gm. in 24 hours. This severe toxic condition was observed in 12 infants. A less severe illness occurred in 17 somewhat older infants of up to 9 months old and a third type of symptomless infection was discovered in 25 children of 1 year or more. There is a full clinical account of the cases and description of the energetic and elaborate treatment employed. All the patients recovered fully. Details are also given of the investigations which were undertaken and of the discovery that a nurse was a chronic carrier of Salm. Thompson. She gave no history of symptoms of an intestinal infection and her carrier state was cured by treatment with chloronitrin.

In the light of this epidemic experience it is considered that there should be bacteriological stool examination of all new admissions to the clinic and all new members of the staff and that such examination should be continued at regular routine intervals. Similar control of milk and food should be carried out with

protection from flies in the warm months. Some points on personal hygiene are also mentioned.

M. E. Delafield

HEATHER, C. D. & NOBLES, Barbara. La salmonelosis en los gatos domesticos. [**Salmonellosis in Domestic Cats**] *Bol. Oficina Sanitaria Panamericana.* 1961, Mar., v. 50, No. 3, 246–9.

The authors, writing from the Department of Public Health at Austin, Texas, point out that while a good deal is known about salmonellosis in dogs little is known at present of the position in cats.

They therefore carried out experiments on groups of cats, feeding to them in some instances dog food purchased in the ordinary way, which had previously been shown to contain *Salmonella* spp. 4 groups of cats, most of which were less than 1 year old, were fed and rectal swabs taken at varying intervals afterwards and plated out after enrichment. In some tests an artificially contaminated food infected just before ingestion was fed to the cats.

The results were: A—purchased dog food:— eaten by groups of 1, 4, 5, and 4 cats respectively for periods of 22 to 48 days (only 1 cat in the latter group); in 10 all swabs were negative, 2 excreted organisms for not less than 18 days. Of 2 groups containing 1 and 4 cats, 1 and 3 cats gave positive swabs respectively; for the group containing 1 cat the foodstuff contained 8 *Salmonella* spp., the cat was positive to 2 of these and 2 others also one of which was *Salm. enteritidis.* In the 2nd group the food contained 9 *Salmonella* spp. and the 3 positive cats had altogether 5 *Salmonella* spp. between them 4 of which were also in the food and 1, *Salm. infantis* was not. The 2 negative cat groups each received 5 *Salmonella* spp. in the food, none of which was common to the other group.

Tests were then made by massive infection to try and produce either a clinical infection or a carrier condition or both, as follows:— group (1), 2 cats; fed with Salm. Newport, 116×10^6, observed for 91 days. 7 and 10 specimens respectively positive, the last 43 days after infection: (2), 3 cats; fed with *Salm. cholerae-suis,* 117×10^6, observed for 62 days; 0, 6 and 2 specimens respectively positive, the last 17 days after infection. (3), 4 cats; fed with Salm. Worthington 121×10^6, observed for 37 days; 7, 9, 9, and 7 specimens respectively positive, the last on 28th day. No clinical symptoms were detected and the authors consider that they were unable to produce a true carrier state.

They are of the opinion that (1) the administration of a low level of salmonellae for several weeks probably does not produce a carrier state in cats even if the organism can be recovered from the faeces; (2) even the administration of large doses does not mean that the animals will necessarily excrete for a longer period; (3) however, since the animals did excrete salmonellae for a certain length of time this may be of public health importance.

[No explanation is given as to why 1 cat was found to be excreting *Salm. enteritidis* not present in the food, nor of the obvious importance of the sale of dog food infected with such well known types as Salm. Newport, *Salm. anatum,* Salm. Minnesota, Salm. Montevideo, etc.]

W. K. Dunscombe

GAUVREAU, L., LAPOINTE, D. & DECHENE, E. Étude du rôle de la mère et de l'enfant nouveau-né dans la dissemination des gastro-entérites à *Escherichia coli* entéropathogènes. [**Study of the Role of the Mother and the Newborn Infant in the Spread of Enteropathogenic *Escherichia coli* Gastroenteritis**] *Canadian J. Pub. Health.* 1961, Jan., v. 52, No. 1, 14–22.

These authors have attempted to relate the carriage by the full-term mother of enteropathogenic *Escherichia coli* to infection of the newborn infant, but only 3% of the 294 mothers examined were found to be excreting these organisms and no more than 3 of the infants born of these mothers were carrying the corresponding serotypes of *E. coli.* Of 415 newborn infants about 12% were found to be excreting one of the recognized enteropathogenic *E. coli* and these excreters were placed under special observation for 10 weeks. During this period just over half of them developed gastroenteritis at some time from the 4th day onwards to the 30th day. Among those who remained healthy there was one who continued to excrete the strain originally isolated on the day of birth for 60 days. It should be noted, however, that the organism isolated from the infants at the time they developed diarrhoea was not always identical with the one they were previously carrying: *E. coli* O 127 was isolated from the stools of every sick child but some of these had been carrying other serotypes. In one of the institutions concerned *E. coli* O 127 was epidemic and sufficiently detailed epidemiological information is not given to explain clearly how this complicated the issue. Since 16 of the healthy infants carried O 127 it is assumed that 17/26 sick children were also previously carrying only this serotype.

H. J. Bensted

HUB, M. Případ antraxu. [**A Case of Anthrax**] *Časopis Lékařů Českých.* Prague. 1960, Nov. 11, v. 99, No. 46, 1456–9, 8 figs. English summary (8 lines).

A description is given of a fatal case of anthrax septicaemia which occurred in Czechoslovakia in 1958, and which was first recognized at autopsy. The patient was a woman aged 40 employed in a brush factory, who developed a febrile illness characterized by cough, fever, abdominal pain, anorexia, vomiting and weakness. She was seen by 3 doctors, and a diagnosis of influenza and neurasthenia was made; death occurred on the 3rd day of illness.

At autopsy there was a haemorrhagic focus 5×10 mm. in size in the left cerebral hemisphere, the peritoneal cavity contained 650 cc. of viscous fluid, parts of the small intestine were haemorrhagic and the adjacent lymph nodes were enlarged, the spleen was enlarged, extensive effusions were present in the pleural cavities and pericardium, a haemorrhagic infiltrate was found in the lungs, and similar changes were present in a

number of other organs. The diagnosis was established by the isolation and identification of *Bacillus anthracis*. The infection may have been derived from bristles imported from China, but attempts to isolate *B. anthracis* from the material were unsuccessful. *D. J. Bauer*

SINHA, B. N. **A New Line in the Treatment of Tetanus.** *J. Indian Med. Ass.* 1961, Apr. 1, v. 36, No. 7, 286–8. [13 refs.]

The author treated 12 patients suffering from tetanus with chlorpromazine, 50 mgm. intravenously or intramuscularly every 12 hours, phenobarbitone 3 grains every 12 hours, prednisone 20–30 mgm. daily for a few days and polyvinyl-pyrrolidone (periston-N) 100–200 ml. intravenously daily for 7 days. 2 patients died, 1 discharged himself otherwise than cured, and 9 were cured. The author was satisfied that further trial of this method was indicated. *A. B. Christie*

SRIVASTAVA, S. P. & CHATTERJI, G. G. **Tetanus.** *J. Indian Med. Ass.* 1961, Apr. 1, v. 36, No. 7, 289–95. [12 refs.]

0·61% of 97,588 patients admitted to S. N. Hospital, Agra, India, between 1952 and 1958 were suffering from tetanus, a total of 602. The authors review the cases from the points of view of age, sex, geography, type and site of wound, incubation period, etc. They also tabulate the results of 12 different treatment regimes but these are not correlated in any way with severity of illness. They plead for mass active immunization. *A. B. Christie*

SYNGAL, K. L. **Tetanus Neonatorum treated without Serum.** *Indian J. Child Health.* 1961, Apr., v. 10, No. 4, 190–94.

In a Bombay practice the author saw 8 patients with neonatal tetanus all of whom died almost without treatment, the cost of tetanus antitoxin being too high for poor parents. Later he decided to treat patients without antitoxin but gave instead phenobarbitone ½ grain orally every 6 hours, cortisone 5 mgm. 3 times daily by mouth and penicillin by injection once daily. Expressed breast milk was given by a medicine dropper into the mouth. On this routine, 4 out of 10 babies survived. *A. B. Christie*

FOSTER, Jean A. & MATZKE, H. A. **The Neurocytology of Experimental Ascending Tetanus.** *World Neurology.* Minneapolis. 1961, Jan., v. 2, No. 1, 22–37, 4 text figs. & 10 figs. (2 coloured) on 5 pls. [30 refs.]

KOWAL, J. **Spirillum Fever. Report of a Case and Review of the Literature.** *New England J. of Med.* 1961, Jan. 19, v. 264, No. 3, 123–8, 3 figs. [14 refs.]

This is an excellent review of a rare and as yet not clearly classified fever. There are 9 known species of motile, spiral, Gram-negative organisms, only one of which, *Spirillum minus*, is a well recognized pathogen and the principal cause of rat-bite fever. The others, which have been isolated from stagnant water, putrefying matter, and sputum, and which, in contrast with *S. minus*, grow readily on artificial media, have been generally considered non-pathogenic for man. In this article, however, a case of recurrent fever with chronic pancytopenia is described, and the diagnosis was supported by blood culture of one of these spirilla; moreover, a summary of the clinical and laboratory data from 6 similar cases described in the literature is reviewed [see, for example, *Trop. Dis. Bull.*, 1944, v. 41, 943]. In none of these cases, with one possible exception, was a history of rat-bite fever elicited, and in all of them an associated illness was present which may have weakened resistance to normally avirulent organisms. The ease with which the spirilla were grown on artificial media made the diagnosis relatively simple. The sensitivity of the organisms to the tetracyclines and chloramphenicol suggests that a cure should be possible in most cases, and indeed the patient discussed responded rapidly to penicillin plus tetracycline when he was admitted to hospital with the complaint for the third time. Untreated patients tend to have recurrent or prolonged irregular fever with involvement of the heart or nervous system.

The morphology of these spirilla is different from that of *S. minus*; they are thicker in diameter, of more variable length, have more coils, and different types of flagellae, undulations, and ends. It is suggested that the term "spirillum fever" be used to include all cases of infection with a spirillum other than *S. minus*. *H. Stanley Banks*

ŠEBEK, Z. Leptospiroseuntersuchungen beim Jagdwild. [**Survey of Leptospirosis in Field Animals**] *Angewandte Parasit.* Jena. 1960, Aug. & Oct., v. 1, Nos. 2 & 3, 52–6; 84–8. [30 refs.]

The English summary appended to the paper is as follows:—

"Serological investigations for leptospirosis were carried out with 1440 specimens of animals (17 species) from the region of Jihlava, which is known as an endemic area of the foci of *Leptospira grippotyphosa, L. sejroe, L. icterohaemorrhagiae* and *L. australis*. Positive reactions were recorded in the sera of the hare (*Lepus europaeus*), musk-rat (*Ondatra zibethica*), fox (*Vulpes vulpes*), ermine (*Mustela erminea*), weasel (*Mustela nivalis*), pole-cat (*Putorius putorius*), badger (*Meles meles*), domestic cat (*Felis domestica*), wild hog (*Sus scrofa*), fallow deer (*Dama dama*), deer (*Cervus elaphus*) and roe-deer (*Capreolus capreolus*). The most frequent ones were the reactions with *L. grippotyphosa*, with which 88·8 p. c. of all positive sera reacted; with *L. sejroe*, 4·4 p. c. were positive, and with *L. australis, L. icterohaemorrhagiae, L. bataviae, L. mitis* and *L. pomona* 3·2, 1·2, 1·2, 0·8 and 0·4 p. c., respectively, of the total of all positive reactions. The highest percentage of serologically positive reactions was detected in the Carnivora (more than 50 p. c.). Only one part of the investigated material could be examined by means of cultivation, and no direct proof of Leptospirae was obtained. From the non-correlation between the

frequent serological positivity and total negativity of direct proof of Leptospirae, the author suggests that the examination of animals for epizootic processes in the natural foci of Leptospirae is worthless."

MACCABE, A. F., CONN, Nancy K. & BOYD, D. H. A. **Meningitis due to *Listeria monocytogenes*.** *Scottish Med. J.* Glasgow. 1961, May, v. 6, No. 5, 199–202, 1 fig. [17 refs.]

BUTTIAUX, R. & VANDEPITTE, J. Les *Flavobacterium* dans es méningites épidemiques des nouveau-nés. [***Flavobacterium* in Epidemic Meningitis of New-Born Infants**] *Ann. Inst. Pasteur.* 1960, Mar., v. 98, No. 3, 398–404. [12 refs.]

A small outbreak in the Congo of meningitis in the newborn infant is described in which a *Flavobacterium* was isolated from the cerebrospinal fluid of 5 patients. The organism appears to be similar to that described by KING [this *Bulletin*, 1959, v. 34, 1182] as responsible for 19 cases of meningitis in premature or full term infants in the U.S.A. and who suggested the name *Flavobacterium meningosepticum*. The mortality among these infants was very high and it seems likely that the newly born infants in the Congo were infected through being bathed in water contaminated with this organism; bacteria having the same characters as those isolated from the cerebrospinal fluid of the infants were cultured from the taps supplying water to the lying-in room of the maternity hospital in which the cases occurred. [The significance of this report seems a little uncertain; a great variety of organisms, especially members of the *Escherichia* and *Salmonella* genera, can cause purulent meningitis in newborn infants under high levels of exposure. Many of the bacteria that have been isolated from the cerebrospinal fluid of such patients would not normally be classified as pathogenic, but the meningeal tissues of the newborn infant would be peculiarly susceptible to infection under heavy exposure. The epidemiological investigations appear to be incomplete with regard to this particular outbreak, but there seems to be, so far, insufficient evidence to show that *Fl. meningosepticum* has peculiar properties that are related to the setting up of meningeal infections in infants.]

[See also this *Bulletin*, 1959, v. 34, 420.]

H. J. Bensted

VIRUS INFECTIONS

The order in this section is:—***General, Psittacosis-Lymphogranuloma group, Pox group, Respiratory group, Reovirus group, Enteric group, Arthropod-borne group, Others.***

DUDGEON, J. A. **Modern Aids to Diagnosis of Virus Diseases.** *Brit. Med. J.* 1961, May 6, 1269–76, 1 diagram & 7 figs. on 2 pls. [49 refs.]

This is a most interesting, thorough and up-to-date account of the laboratory methods of diagnosis of virus diseases. It should be read by anyone desirous of making use of the facilities of a diagnostic laboratory. The subject is considered under the 3 main lines of investigation available.

(i) Microscopy: This can be used to recognize virus elementary bodies, for cytological studies of exfoliated cells and for histological studies of tissue obtained at biopsy or autopsy. The method may enable a rapid provisional diagnosis to be made, but it lacks sensitivity and requires confirmation by other methods.

(ii) Virus isolation: This is a method that has greatly increased in versatility and power with the advent of tissue culture methods, but older techniques involving inoculation of eggs and mice, particularly suckling mice, still remain the methods of choice for some viruses. Viruses in tissue culture can be recognized by cytopathic effects causing cell destruction seen under the microscope, as a plaque of degeneration under agar or by metabolic inhibition. Viruses may also be recognized by haemagglutination or haemadsorption or the antigen can be detected by the fluorescent antibody technique or by complement fixation.

(iii) Serological tests: These are the most commonly used and generally valuable method. They can be used to detect viral antigen in tissues taken fom the patient but at present are only commonly used in this way for smallpox, or for serum antibody titration. Smallpox-vaccinia antigen can be detected by complement fixation or gel diffusion in agar. Serological methods have severe limitations. First, 2 serum specimens are required, making the diagnosis retrospective. Second, the multiplicity of serological types of virus is a severe limitation fortunately helped by the presence of group antigens with influenza and adenoviruses for example. Third, the interpretation of serological results depends upon adequate liaison between clinician and virologist. The various methods of serological diagnosis (virus neutralization, complement fixation and haemagglutinin inhibition and fluorescent antibody) are briefly reviewed.

Finally, the power of these methods is illustrated by reference to experience in the diagnosis of paralytic poliomyelitis and non-paralytic poliomyelitis. The challenge of the aetiology of rubella and hepatitis remains.

[Dr. Dudgeon does not specifically mention the need for close personal contact between clinician and virologist although since he combines both interests he is well aware of this need. Indeed, he has done as much as anyone in Britain to achieve this desirable liaison; without it a virus diagnostic laboratory will never yield its full potential value.] *A. J. Beale*

VOSTI, G. J. & ROFFWARG, H. **Myocarditis and Encephalitis in a Case of Suspected Psittacosis.** *Ann. Intern. Med.* 1961, Apr., v. 54, No. 4, 764–76, 5 figs. [39 refs.]

CHARKES, N. D. **Purpuric Chickenpox: Report of a Case, Review of the Literature, and Classification by Clinical Features.** *Ann. Intern. Med.* 1961, Apr., v. 54, No. 4, 745–59, 1 fig. [87 refs.]

MÉLENDEZ, L. Aislamiento e identificación de virus de fiebre aftosa procedente de vesículas en la epidermis de un ser humano. [**Isolation and Identification of Foot and Mouth Disease Virus from Skin Vesicles in a Human Being**] *Bol. Oficina Sanitaria Panamericana.* 1961, Feb., v. 50, No. 2, 135–7.

The English summary appended to the paper is as follows:—

"1. A cytopathogenic agent for bovine kidney cells isolated from hand vesicles of a human being.

"2. This agent is pathogenic for bovine kidney cells *in vitro,* guinea pigs and suckling mice.

"3. This agent belongs immunologically to the 'O' type foot and mouth disease virus.

Discussion

"In spite of the fact that the patient has been working for over 10 years with foot and mouth disease viral materials, she never before presented similar symptoms. A search for heterologous antibodies produced by inapparent or subclinical infections was made. Neither the acute nor the convalescent sera, when diluted 1:8, revealed the presence of antibodies against A and C type foot and mouth viruses.

"This brief paper shows the possible existence in nature of some peculiar foot and mouth virus strains, which, in some special circumstances, could infect man.

Conclusions

"The fluid from a hand vesicle of a human, produced destruction in bovine kidney cultured cells. In this way a cytopathogenic agent has been isolated *in vitro.* The specific inhibition of cellular destruction by this agent in the presence of 'O' type hyperimmune guinea pig serum proves that this agent belongs immunologically to the 'O' type foot and mouth disease virus.

"It is the first time that a foot and mouth disease virus from a human has been isolated in bovine kidney cells cultured *in vitro.*"

WATSON, G. I. **The Clinical Epidemiology of Influenza.** *J. College General Practitioners.* 1960, Feb., v. 3, No. 26, 44–79, 16 figs. [22 refs.]

This is a most creditable piece of epidemiological detective work by a general practitioner in a rural area. By observation and record keeping after the manner of William Pickles of Aysgarth, and with laboratory support, he studied 307 patients in 176 families during the Asian influenza epidemic of 1957.

He presents evidence of the spread of the infection in typical, atypical, and symptomless forms within households, and of the effectiveness of isolation in a single room of a house in a few cases. The incubation period as judged by the time of onset in secondary cases, seemed to be constant at 2–2½ days. Infectivity was strongly correlated with fever, except when antipyretic drugs were used, even up to a week or more from the onset of symptoms; the virus was isolated in 8 out of 10 specimens from the upper respiratory tract when the temperature was 100°F. or more at the time of sampling, but at lower temperatures all 11 attempts to isolate virus were negative.

Acute observation indicated that it was coughing that particularly spread the infection; the secondary attack rate from patients without a cough was only about half of that from patients with cough and other symptoms. Patients exhibiting a diphasic type of temperature were deemed to have been reinfected with virus released from their own respiratory tract during the first bout of fever, the incubation period of this second wave of pyrexia being the same as that in an ordinary secondary case (2–2½ days).

The author and his partner remained free from clinical symptoms throughout the 6-month period of the epidemic, but 4–6 weeks after the start of it both developed a rise and subsequent fall in complement-fixing antibodies against virus influenza A—clear evidence of symptomless infection. *H. Stanley Banks*

NOVACK, A. & FELDMAN, H. A. **Outbreak of Asian Influenza in College Students.** *New England J. of Med.* 1961, Apr. 13, v. 264, No. 15, 743–7. [16 refs.]

An outbreak of influenza occurred in February 1960 among students of Syracuse University, New York. Influenza virus type A2 was shown to be responsible. The virus was isolated from the throat swab or gargle in 20 of 41 patients tested. From the same 41 students, paired sera were available from 39 and a 4-fold or greater rise was shown in 18, 13 of whom also had demonstrable virus. Initial haemagglutination—inhibition titres of 1 in 40 or more were found in 61%, indicating previous experience with the virus, very different from the pre-1957 era when only people over 60 years old were shown to have had such experience. The outbreak was limited to only a few weeks and this previous experience with the virus may have helped to limit the spread among students. *A. B. Christie*

DELANOE, G. Un cas de péricardite grippale à virus Sing. A. [**A Case of Influenzal Pericarditis due to Sing Virus**] *Bull. Soc. Path. Exot.* 1960, Nov.–Dec., v. 53, No. 6, 925–9, 3 figs. on 2 pls.

HEASMAN, M. A. & REID, D. D. **Theory and Observation in Family Epidemics of the Common Cold.** *Brit. J. Preventive & Social Med.* 1961, Jan., v. 15, No. 1, 12–16. [10 refs.]

Attempts to test hypotheses about the spread of infectious disease within a community are usually handicapped by a lack of sufficient data in adequate detail, particularly about epidemic behaviour within families. An investigation of respiratory illness in a series of families by BRIMBLECOMBE, *et al.* [this *Bulletin,* 1958, v. 33, 311] provided the present authors with appropriate data to overcome this difficulty. They compared the observed spread of acute coryza—or common cold—in a series of families each of 2 parents and 3 children with that expected from 3 theoretical models.

The theoretical models used were: (1) GREENWOOD's [*ibid.,* 1931, v. 6, 801] well known "chain binomial"

theory. This assumes a relatively short infectious period, a relatively long and stable incubation period and the effective removal of susceptibles from circulation as they become infected. (2) REED and FROST's (cited by BAILEY, *The Mathematical Theory of Epidemics*, 1957, London, Griffin) model, which although based on the same arguments and assumptions as Greenwood's also allows for the chance of infection at any given stage of the epidemic being dependent upon the number of infective persons then in circulation and to whom the remaining susceptibles are exposed. (3) BAILEY'S [this *Bulletin*, 1956, v. 31, 106] model based on the idea of a constant ratio of rate of infection to rate of "removal" (*i.e.* by death, isolation, recovery, etc.) of susceptibles. Thus this "continuous infection" model does not presuppose the short period of infectiousness inherent in the others.

Each family was visited fortnightly and a time chart was prepared to show for each of its 5 members the date of onset and type of respiratory illness. New or primary infections of acute coryza were defined as those with onsets occurring after an interval of at least 10 days since the last such onset in the same family. 2 primaries on the same or succeeding days were defined as multiple primaries. The criterion of this 10-day interval was fixed before any time charts were studied and was based on the presumed incubation period.

There were 664 families with single primaries and the observed numbers of families with 0, 1, 2, 3 and 4 further cases in the first stage of the family epidemics were 423, 199, 39, 3 and 0 compared with 420·91, 203·18, 36·79, 3·05 and 0·07 expected by models (1) and (2) above. The agreement is excellent ($0{\cdot}7 > P > 0{\cdot}5$) with a probability of transfer of 0·108. Examination of the data in subgroups classified by the family status (father, mother, school child or pre-school child) of the first affected did not materially disturb the goodness of the fit of observed to theoretical distributions. The probabilities of transfer when infection was introduced by a father, mother, school child or pre-school child were 0·111, 0·086, 0·128 and 0·095 respectively and these have been discussed by Brimblecombe *et al.* [*ibid.* 1958, v. 33, 311]. In the complete family epidemics with single primaries the observed and expected (by models (1) and (2) in that order in brackets) distributions of families were 423 (405·3, 409·9) with 0 further colds, 131 (147·1, 146·3) with 1, 60 (79·3, 68·9) with 2, 36 (31·0, 24·4) with 3 and 14 (1·2, 14·4) with 4. The Reed-Frost model gives a better fit ($0{\cdot}05 > P > 0{\cdot}02$) than the Greenwood model ($P < 0{\cdot}001$) but neither is very good. When, however, these data were subdivided by housing conditions the Reed-Frost model is much more satisfactory for all 3 sub-groups, "overcrowded", "crowded" and "uncrowded" for which the probabilities of transfer were 0·124, 0·118 and 0·101 respectively. However, Bailey's model also described these data fairly well and is as good, if not better, for "overcrowded" and "crowded" families.

The success of this exercise should encourage further work in this field both in the postulation of new hypotheses and the collection of suitable data with which to test them. The present application of models based on different assumptions has resulted in goodness of fit being apparently influenced by enviromental differences between the sub-groups examined and further results of this kind could lead to a better understanding of epidemic processes.

E. A. Cheeseman

LOCKHART, R. **Treatment of the Common Cold by Terramycin.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1961, Jan., v. 19, No. 1, 12–13.

Treatment of the common cold with antibiotics on the first and second days of the disease seems to be helpful both in relieving symptoms and in reducing the time lost from work. A trial was carried out by the medical officer of the British Aluminium Co. on 202 members of the staff of 3 Scottish factories, all of whom reported with a cold within 24 hours of the onset of symptoms. Two troches, each containing 30 mgm. oxytetracycline, were taken night and morning for 2 days—a total dose of 240 mgm. of the drug. The trial was uncontrolled, but the findings were compared with those experienced with former colds, as stated by each of the participants when reporting.

The results showed a larger proportion "cured" in 4 days as compared with former experience—45% against 8%— and the percentage of patients who lost no time at work was 92, the figure in former years being 72.

There were 35 people (excluded from the trial) who did not start treatment until 24 hours or more after the onset of symptoms; these did not appear to obtain any benefit at all from the treatment.

H. Stanley Banks

GUÉPIN, J. P., JANSON, P., KRUIMEL, J. P. & LORENZEN, H. Die Behandlung der Grippe und Erkältung, des Schnupfens und verschiedener anderer Viruskrankheiten bei Menschen, Tieren und Pflanzen. **[The Treatment of Influenza, Colds and Other Virus Diseases of Man, Animals and Plants]** *Arch. f. Hyg. u. Bakt.* 1961, Mar., v. 145, No. 2, 88–107, 2 figs. [15 refs.]

Pyridacil (Pyridium, 3-phenyl-azo-2, 6-diaminopyridine hydrochloride) was used independently by 3 doctors in the 1930's for the treatment of infection of the urinary passages when it was observed that concurrent, early conditions of influenzal and catarrhal character rapidly disappeared in a remarkable way.

The authors of this paper, who include the 3 doctors mentioned, here report in detail on the promising results they and 67 medical practitioners have observed in the treatment of hundreds of early cases of influenza with pyridacil. For example, of 975 patients suffering from early influenza 920 were rapidly cured, as judged by the temperature and symptoms, and all were able to get up on the third day and most returned to work on the fourth day. In a control group of untreated patients the return to work had to be delayed till the 6th–9th

day. Good results in the treatment of simple coryza are also recorded. Much space is also devoted to description of and references to the value of pyridacil in measles and chicken-pox, in virus disease of pigs, in herpetic stomatitis and keratitis and in some virus infections of tobacco and tomato plants.

M. E. Delafield

Sales-Vázquez, R. & Espadaler-Medina, J. M. La epidemiología de la poliomielitis en España. [**The Epidemiology of Poliomyelitis in Spain**] *World Neurology*. Minneapolis. 1961, Jan., v. 2, No. 1, 13–21, 5 figs. English summary.

Although the first reported cases of poliomyelitis in Spain occurred in Tarragona in 1896 none were found subsequently till the second decade of this century when successive epidemics occurred, including an outbreak in Barcelona in 1917. In 1931 all transmissible diseases were made notifiable and this paper really describes the course of poliomyelitis in the last 30 years.

The authors point out that the figures given refer only to the paralytic form and that no statistically significant numbers of serological tests have been carried out, but that it has been adequately demonstrated that the infection is prevalent in all parts of the country, with short, sharp epidemics at lessening intervals but with increasing intensity and gravity each time.

The number of cases notified from 1931 to 1959 is given in a table (the figures for 1936–39 are omitted because of the civil war). From this it appears that in the decennium 1950–59, in only 4 years were less than 1,000 cases notified (and 2 of these had over 900) while 1959 had the highest figures of all time—2134 cases, a rate of 7·05 per 100,000. Here the authors point out that while between 1931 and 1950 the notifications have doubled every 8–12 years, in the decennium 1950–59 they have doubled in rather less than 8 years.

In general the causes of the increased incidence are considered to be similar to those of other countries but mention is made of the improvement in the general sanitary conditions leading to a reduction in infant deaths while at the same time there is an increased incidence of poliomyelitis. As an example of the sharp outbreaks that occur, Barcelona is quoted, where in 1959 there were 298 notified cases with 102 deaths.

Although cases do occur throughout the year the greatest incidence (78%) is in June to September. Most are in the coastal areas, and this might be due to the considerable climatic differences between the coastal and central areas, but is better explained by the fact that except for certain cities, notably Madrid, the central area is much more sparsely populated. There is no difference in sex incidence and there seems to be an increasing tendency for persons over the age of 5 to become affected.

The increased incidence is regarded as due in part to the almost geometrical increase in population; dissemination of the virus occurs early and the infection is probably acquired in the first 2 years of life. The resulting endemicity tends to maintain a relative state of immunity among the adult population due to single or successive sub-clinical re-infections. There has, however, been an increase in the case fatality rate in the more recent outbreaks, owing to the greater gravity of the clinical forms. In the 1959 Barcelona epidemic, for example, though 131 cases occurred in children under 2 the case fatality rate was not more than 24·2%, while in adults aged 21–30 there were 7 cases with 2 deaths and in the 31–40 group 7 cases with 5 deaths. In this outbreak more than 30% of the patients were affected at higher levels. Unfortunately the proportion of spinal, bulbo-spinal, bulbar, and encephalitic forms cannot be stated exactly, since numbers of patients with the less grave spinal forms are nursed at home. However in 1,000 treated the paraplegic form was the most common.

W. K. Dunscombe

Rindge, Mila E. **Poliomyelitis in Connecticut—1960.** *Connecticut Health Bull.* 1961, Apr., v. 75, No. 4, 111–14.

In Connecticut in the 5 years 1951–55 there were on the average over 400 cases of, and 17 deaths from, poliomyelitis per year. In the 5 years 1956–60, following the widespread use of Salk vaccine, the corresponding averages were approximately only 60 cases and 4 deaths. Of the 36 attacks reported in 1960, 19 were in children aged 5 or less, only 7 were in the best-vaccinated age-group 6–19 years and 10 were in adults 20 or more years of age. The geographic distribution was striking and unusual with as many as 20 of the 36 cases occurring in towns close to the Rhode Island state boundary and inhabited by less than 5% of the population of Connecticut. A severe epidemic took place in Rhode Island and doubtless provided the focus of infection. The lack of protection sometimes following a full course of Salk vaccine is shown in 15 persons who had had 3 or more injections of whom 4 died (children aged 2, 4, 5 and 5). Type I was the predominant organism in 1960 though Type III virus was also isolated.

A. Bradford Hill

Ravenholt, R. T. **Poliomyelitis in an Immunized Community: Seattle-King County, Wash., 1959.** *Pub. Health Rep.* Wash. 1961, Feb., v. 76, No. 2, 166–78, 4 figs. [28 refs.]

From 1948 to 1953 reported cases of poliomyelitis in Seattle-King County, Washington, were annually at the high level of 20 or more per 100,000 population. Coincident with intensive application of Salk vaccination a rapid decline occurred and in 1956–58 there were very few cases and no deaths. During the period June to December 1959, however, a sharp increase occurred and there was a return to an attack rate of nearly 13 per 100,000 (due to type 1 virus) although a survey in the previous May had revealed that about 93% of all elementary schoolchildren had received at least 3 doses of vaccine. In the poorest school districts, however, less than half the kindergarten children were protected on entry to school.

While the seasonal distribution was normal there was an unusual geographical spread, a freedom from attack

in the upper socio-economic residential areas, and an unusual age distribution showing a relatively large proportion of adult patients (59% of the total). 85% of the patients were either pre-school children or lived in households with pre-school children. 65% had received no Salk vaccine prior to onset and another 18% had had only one or two doses. On the other hand there was no appreciable difference between the fatality rates for unvaccinated patients (6·8%) and triply vaccinated patients (5%) and in the proportion of patients with severe residual disability (30 and 25%). (The one triply vaccinated patient who died had completed an optimumly spaced series 18 months before onset.)

No unusual or suggestive association of cases with water, milk, food, physicians, dentists, insects, injections or travel was observed. Bulbar paralysis was not significantly associated with previous tonsillectomy. It is concluded that the outbreak was probably due specially to an accumulation of an unusually susceptible pre-school population in public housing projects and similar low socio-economic groups. This accumulation indicates a lack of natural immunization which, with the very low incidence of poliomyelitis in the previous 3 years and the epidemic changes in racial, socio-economic and geographical distribution of cases, suggests that the extensive use of Salk vaccine had (contrary to general belief [see Fox *et al.*, this *Bulletin*, 1959, v. 34, 112]) temporarily limited the propagation of poliovirus in the community. *A. Bradford Hill*

Depoux, R. & Chambron, J., with the technical collaboration of Mlle. Baldasar. Enquête sérologique sur l'incidence de la poliomyélite chez les singes sauvages de la République du Congo. [**Serological Study on the Incidence of Poliomyelitis in Wild Monkeys in the Congo (Equatorial Africa)**] *Bull. Soc. Path. Exot.* 1960, Sept.–Oct., v. 53, No. 5, 781–4.

A survey of antibodies to poliovirus was made in 130 monkeys of 12 species. 42 contained antibodies to all 3 types and 5 had antibodies only to type 3. In addition 3 chimpanzee sera were tested and found to have antibodies to all 3 types of poliovirus but these animals had been captive for some time. *A. J. Beale*

Ormiston, G. **The Prophylaxis of Acute Poliomyelitis.** *Practitioner.* 1961, May, v. 186, 602–9. [34 refs.]

A general account.

Földes, P., Szeri, Helen & Bános, Susanna. **Antigenicity and Stability on Storage of Salk Type Vaccines produced in Hungary and Abroad.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 3, 211–14.

Killed poliovaccine stored at 4°C. and between 21° and 23°C. for 2 weeks did not lose potency as judged by the antigen extinction test in guineapigs. Hungarian vaccine appeared as potent and as stable as foreign vaccine. *A. J. Beale*

Harvey, W. C. **Poliomyelitis Vaccination. Experience in a Middlesex Area.** *Med. Officer.* 1961, Feb. 24, v. 105, No. 8, 103–7, 1 fig.

This paper describes the teething troubles which occurred, at the time when vaccination against poliomyelitis was introduced in 1956, in certain areas of Greater London in the county of Middlesex, and how they and later difficulties were overcome.

There was in 1956 confusion and some anxiety among the people because the unfortunate accidents which were reported from California when the Salk vaccine was first used were fresh in their minds. Their reluctance was overcome by appropriate publicity and alarm was allayed as more and more children were vaccinated without untoward effect and figures became available to demonstrate that the vaccine was of value. A more serious obstacle was the periodic shortage of vaccine and the need to ration what was available at any particular time. This was done by inviting the parents of children in prescribed age-groups to register for vaccination. After the scheme for vaccinating at local authority clinics had been in operation for a few months, vaccine was issued to general medical practitioners for use for children in the eligible age-groups. In September 1957 the Government decided to supplement the British vaccine by importing Salk vaccine from North America provided that it was retested in Britain. At that time the age for eligibility was raised to 15 years but the parents were given the right to choose which type of vaccine, British or American, should be used. It was only in May 1958 when the requirement that American vaccine must be retested here was dropped temporarily that vaccine became available for all children whose parents asked for it: they were still given a choice but if they wanted one in short supply they had to wait. In July 1958 the age limit was increased to 25: expectant mothers of any age had already had a high priority.

At this stage publicity for the recruitment of candidates for vaccination was renewed and extended to the local press and any voluntary organizations likely to be helpful. The need for prior registration was abandoned. There was an upsurge of demand and vaccination sessions on Saturday mornings were started by the local authority. Those who could attend only in an evening were catered for by general practitioners.

The demand was falling when it sprang to life again following the much publicized death from poliomyelitis of a well-known footballer.

In February 1960 everyone under 40 became eligible together with a few special groups of any age.

The final result is that about 80% children have been vaccinated and about 50% of the adults under 40 years of age. Adults over 40 can now be included for vaccination by a general practitioner but for those outside the priority groups the vaccine is obtained on an ordinary National Health Service prescription instead of from the local authority.

The moral to be drawn from all this is that endless difficulties arise when people have to be persuaded to do something and after they have agreed they have to wait a long time because the requisite material is unavailable. *Allen Daley*

SANTOPADRE, G., CASAROSA, S., RUSCHI, A. & ZERBONI, R. Sulla durata nel tempo della risposta anticorpale a vaccino antipoliomielitico (tipo Salk) in un gruppo di bambini della Provincia di Pisa. [**The Duration of the Antibody Response to a Salk Type Poliomyelitis Vaccine in a Group of Children in the Province of Pisa**] *Riv. Istituto Sieroterap. Ital.* 1961, Jan.–Feb., v. 36, No. 1, 40–54. English summary (7 lines).

This is a study on children aged between 1 and 14 years, 49 of whom had received Salk vaccine 18 months before and 59 two years before. Through the 3 years of this investigation, there were 21 cases of poliomyelitis in the environment (12 of type 1, 2 type 2, 2 type 3, 5 undetermined). Blood samples had been taken (1) before the first injection, (2) 1 to 2 months after the third injection and (3) either 18 months or 24 months after the beginning of treatment (12 or 18 months after the last dose of vaccine).

The findings, on neutralization basis, are given in 16 fully detailed tables. These show that the immunity induced persisted to a high degree up to the time of examination, that it was positively related to the vaccine and independent or any possible concurrent natural factors, the degree of correlation being highly significant statistically. The best results were those related to type 3 when the third blood sample was considered, while this had not appeared to be the case from the second sample just after the end of vaccination. While the antibody rises in the interval had been small as far as type 1 and 2 were concerned, they were very well marked for type 3. The percentage of subjects who showed a high degree of type 3 immunity rose from 53·07 to 91·84 in those sampled after 18 months, and from 30·51 to 89·94 in those sampled after 24 months. If confirmed, these findings prove the antipoliomyelitis vaccine even better than it appears to be on single neutralizing antibody estimations. It is possible that subjects who appear not to respond to the immunogenic stimulus do so later when natural minimal stimuli produce a booster effect. *E. Agius*

BAKÁCS, T. **Poliomyelitis Prophylaxis in Hungary.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 3, 329–36, 4 figs. [14 refs.]

Salk poliovaccine was used extensively in Hungary in 1957 but in November 1959 it was decided to change to the Sabin attenuated poliovaccine for mass prophylaxis. There was an extensive epidemic in 1957 which is thought to have been curtailed by the killed vaccine programme [this *Bulletin,* 1959, v. 34, 113]. 1958 was a year when few cases occurred and this is ascribed to extensive use of Salk vaccine, the immunizing effect of the 1957 epidemic and the interfering effect of an extensive Bornholm disease (Coxsackie B3) epidemic. In the early part of 1959 a third dose of killed vaccine was given. Later in the year there was a severe epidemic but the incidence was much lower in triply vaccinated persons. Data are presented showing that Salk vaccination does not prevent virus multiplication in the gut but does reduce the duration of excretion. The authors conclude that killed vaccine is effective, but that the duration of effectiveness is short and that living vaccine is superior.

[The reviewer does not think either the optimism or pessimism about Salk vaccine is justified by the evidence presented.] *A. J. Beale*

STARKE, G. & WELKE, C. Immunologische Untersuchungen an einem Impfkollektiv bei Polioschutzimpfung mit inaktivem (Salk) und lebendem Impstoff (Sabin). [**Investigation of the Immunizing Response to Inactive (Salk) and Living (Sabin) Poliomyelitis Vaccine**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1961, Feb., v. 7, No. 2, 141–6.

The investigation described here with detailed tables of its results was carried out on 21 adult persons to study their immunizing response to 3 subcutaneous injections of Salk vaccine given during 6 months followed by 3 oral administrations of Sabin vaccine of Types I Lsc 2ab, III P712, CH, 2ab, and II Leon, $12a_1b$ at intervals of 3 weeks. Some particulars are given of the techniques used in serum neutralization tests and virus studies of faecal specimens.

It was shown by the determination of neutralizing antibodies that both vaccines had a good antigenic effect. The high antibody concentration brought about by the Salk vaccine was not, however, increased appreciably by the subsequent administration of Sabin vaccine.

Virus excretion investigation showed that the live virus strains in the vaccine were capable of multiplication but that there was no demonstrable correlation between the level of immunity and the extent of virus excretion. *M. E. Delafield*

WIESMANN, E. Resultate der oralen Poliomyelitisschutzimpfung in der Nordostschweiz. [**Results of Oral Vaccination against Poliomyelitis in North-East Switzerland**] *Schweiz. med. Woch.* 1961, Jan. 7, v. 91, No. 1, 11–12.

Between December 1959 and May 1960 trivalent oral poliomyelitis vaccine was given to 37,600 persons in Switzerland, mostly children of school and pre-school age. Sera were obtained before and 8 weeks after vaccination from 630 persons, 280 of whom were found to have neutralizing antibody to all 3 types of virus before vaccination. Of 83 who were triply negative, 78 (94%) developed a 4-fold or greater rise of titre of neutralizing antibody to type 1 virus, 26 (31%) to type 2 and 80 (96%) to type 3. Among 205 who were initially negative to type 1, an antibody response to the same type occurred in 198 (96·5%), and the

corresponding figure for type 2 was 44% (77 of 176), and for type 3 96·5% (231 of 239). In an examination of stool specimens from 441 persons who developed a significant rise in antibody titre in response to vaccination, poliomyelitis virus could be isolated from 305 persons (70%) 10 days after vaccination, from 119 (27%) after 30 days, and from 18 (4%) after 60 days.

D. J. Bauer

LEVINE, Sonnia, GOLDBLUM, N., MOSCOVICI, O. & HORETZKY, R. **A Small-Scale Field Trial with a Type 3 Attenuated Poliovirus in a Communal Settlement.** *Amer. J. Hyg.* 1961, Jan., v. 73, No. 1, 10–19, 6 figs. [18 refs.]

23 children living in a communal settlement (452 members including 132 children under 13) at Kibbutz Gat in Israel were given 0·5 ml. of the Lederle type 3 living poliovaccine (titre $10^{6·5}$ TCD50/ml.). 22 became infected. All had had a full course of Salk vaccine and had antibodies of 1 in 8 or more to type 3 virus. Type 3 poliovirus excretion usually started after 2 to 3 days and persisted for 1 to 7 weeks. Excretion was longest in young children. 8 months later 22 of the children were given type 3 virus again and only 7 became re-infected. [The duration of infection in these children is not stated.] Contact infections were common; 70% of the contact children aged up to 2 years became infected. Older children and adults were progressively less likely to become infected by contact. The only child who did not become infected was excreting an unidentified virus which presumably interfered with poliovirus vaccine strain. 2 other children were successfully infected despite the prior excretion of an enterovirus (both unidentified). *A. J. Beale*

STERN, H. **Aetiology of Central Nervous System Infections during Prevalence of Poliovirus and Coxsackie Virus. Some Clinical Manifestations of Coxsackie Virus Infections.** *Brit. Med. J.* 1961, Apr. 15, 1061–6. [31 refs.]

In 1959, from 62 specimens of faeces from patients suffering from paralysis, poliovirus type 1 was isolated in 52 and type 3 in 1: the rest were negative. From 93 specimens of faeces from patients suffering from aseptic meningitis, poliovirus type 1 was isolated in 18 and type 3 in 1, Coxsackie virus B4 in 5 and ECHO viruses in 2; 3 other cases were diagnosed serologically as poliomyelitis and 9 as mumps. In 1960, 24 paralytic cases were investigated; from 6 poliovirus type 1 and from 11 poliovirus type 3 were isolated, 2 cases being due to Coxackie virus type B2 and 2 to type B5. From faecal specimens from 115 cases of aseptic meningitis, poliovirus type 1 was isolated in 1 and type 3 in 3, Coxsackie viruses were isolated in 29 and ECHO virus type E9 in 3; 10 other cases were diagnosed serologically as mumps; of 11 cases of meningoencephalitis, 1 was shown to be due to Coxsackie virus B2 and 2 to mumps. It is clear, then, that a different virological pattern was present in the 2 years, even in paralytic cases; in 1959, poliovirus type 1 accounted for 88% of all the virus isolations, in 1960 for less than 12%. Most of the cases of abacterial meningitis due to Coxsackie virus infection showed no unusual features but there were a few exceptions. 2 patients showed a macular rash and 2 had conjunctivitis: the 4 paralytic cases all had mild paralyses although 2 had slight residual weakness: 2 infants had febrile attacks with convulsions but with normal cerebrospinal fluids; one man had a severe relapsing form of meningeal irritation with disorientation followed by facial paralysis and limb paraethesia. Several infants had severe illness with signs of myocarditis and 1 child had croup requiring tracheotomy. [This is a paper full of interesting epidemiological and clinical facts.] *A. B. Christie*

DOMOK, I., MOLNAR, E. & FARKAS, E. **Virological Investigations of Pleurodynia (Bornholm Disease) in an Epidemic in Hungary in 1958 and an Outbreak of Neonatal Myocarditis.** *Problems of Virology.* London. 1960, v. 5, No. 3, 351–7. [Translated from Russian.]

In 1958 there was an extensive outbreak of Bornholm disease in Hungary. 68% of a sample of the patients with symptoms of pleurodynia excreted Coxsackie B3 virus, whereas only 22% of the patients with other symptoms did so. During the epidemic there was an outbreak of myocarditis among newborn infants in the obstetric ward of a hospital in Tataban. 9 out of 12 children suffered from fever and there were signs of myocarditis in 4. 1 infant died. Coxsackie B3 was recovered from the faeces of 8 infants and also from autopsy specimens from the fatal case. 3 children, who were asymptomatic, were among those to excrete Coxsackie B3. *A. J. Beale*

REITANO, G. & DARDANONI, L. Enterobatteri ed Enterovirus in casi di diarrea infantile in Sicillia. [**Enterobacteria and Enteroviruses in Infant Diarrhoea in Sicily**] *Riv. Istituto Sieroterap. Ital.* 1961, Jan.–Feb., v. 36, No. 1, 28–39. [16 refs.] English Summary.

With the purpose of finding whether some, at least, of the cases of infant diarrhoea in Sicily were attributable to ECHO viruses, 196 children under 2 years, mostly from middle-class families in Catania and the central and eastern provinces were studied, between August and October 1959; 139 suffered from diarrhoea, while 57 were controls. Cases were classified as (1) acute and slight, (2) acute and severe, and (3) chronic and slight.

Two rectal swabs were taken in each case, both moistened in Hank's solution. One was shaken up in the solution with antibiotics, and then preserved at − 20° C. The second served for examination for bacterial pathogens including the pathogenic *Escherichia coli* types, carried out on standard lines. Viruses were sought by monkey kidney culture with haemagglutination tests for those showing cytopathogenic effects, followed by haemagglutionation inhibition with anti-ECHO sera and neutralization tests on tissue cultures.

Viruses which were not haemagglutinating were identified by neutralization tests in tissue cultures by anti-ECHO and anti-Coxsackie specific sera. Samples which were not cytopathogenic were inoculated in suckling mice and studied further.

No shigellae or salmonellae were found. 56 strains of pathogenic *E. coli* including O 25 and O 44 were met with, 7 of them in the control group, 5 of the patients with diarrhoea showing the presence of 2 serotypes. O 25 and O 86 gave 10 cases each in a total of 49. Monkey kidney culture showed the presence of 49 cytopathogenic agents; 44 of them were poliovirus 1 and 3, ECHO 6, 7, 8, 11, 19, 21, 22, Coxsackie B1, B3 and B4, while 5 were unidentified. Suckling mice inoculation showed the presence of 6 other pathogens not active in adult mice or in tissue cultures. 37 of the viruses were isolated from cases of diarrhoea, 18 from the controls. From 9 cases of diarrhoea and from 4 controls there was simultaneous isolation of a viral agent and a pathogenic *E. coli* strain.

The authors point out that while pathogenic *E. coli* play an important part, viruses do not seem to do so, being isolated practically equally from patients and controls. This latter finding differs from that of other workers [this *Bulletin*, 1958, v. 33, 1115; 1959, v. 34, 320], the divergence being tentatively attributed to the fact that enteroviruses do not always cause acute infections, and their pathogenicity may not become apparent in environments where there is much interchange of viruses. *E. Agius*

KRAUS, N. & AZZOLA, E. Über den Polimorphismus der Coxsackieerkrankungen. [**Polymorphism of Diseases due to Coxsackie Viruses**] *Ztschr. f. ärztl. Fortbildung.* 1961, Apr. 1, v. 55, No. 7, 343–7. [64 refs.]

LENNETTE, E. H., SHINOMOTO, T. T., SCHMIDT, Nathalie J. & MAGOFFIN, R. L. **Observations on the Neutralizing Antibody Response to Group B Coxsackie Viruses in Patients with Central Nervous System Disease.** *J. Immunology.* 1961, Mar., v. 86, No. 3, 257–66.

This is a valuable study of the neutralizing antibody test on paired sera for the diagnosis of Coxsackie B virus infections. The titrations were performed by using FL human amnion cells in a metabolic inhibition test. A Coxsackie B virus was isolated from 238 of 540 patients with various central nervous diseases and serological evidence of infection was obtained in 50% of the 238. Coxsackie B virus neutralizing antibodies appear early in infection and persist, reducing the value of the neutralization test for diagnosis. When the titre of the acute phase specimen was less than 1 in 32 a 4-fold rise occurred in 70–80% of the cases, whereas such a rise was rarely observed when the acute phase titre was over 1 in 32. Coxsackie B neutralizing antibodies were prevalent, and heterotypic boosts to antibody titres occurred. *A. J. Beale*

CRAMBLETT, H. G., WILKEN, F. D., LANGMACK, Marcia & PORTER, Joyce. **Patterns of Transplacental Transfer of Neutralizing Antibodies against ECHO Virus Types 1, 2, 8, 11 and 20.** *Amer. J. Hyg.* 1961, Jan., v. 73, No. 1, 90–95, 7 figs.

Sera were obtained from mothers at the time of delivery and from their infants' cord blood. The content of neutralizing antibodies to ECHO viruses 1, 2, 8, 11 and 20 and complement-fixing [CF] antibodies to adenovirus were determined. It was found that adenovirus group CF antibodies were equal to or greater than maternal titres in the cord sera but that almost always ECHO virus neutralizing antibody titres were less in cord sera. The incidence of previous ECHO 11 and 2 infections among pregnant women was greater than for ECHO 1, 8 and 20. In a study of sera from children and adults it was found that the prevalence of ECHO 20 antibodies exceeded that of ECHO 8. There was a similar pattern of higher levels in children under 6 months with a low point at 1½ to 3 years rising to a peak later, though for both viruses there was a dip in antibody prevalence in children between 12 and 15 years. The incidence of antibodies in those over 15 was about 10% for ECHO 8 and about 30% for ECHO 20. *A. J. Beale*

MANNING, R. T., WEBER, R. W. & DELP, M. **Infectious Hepatitis: the use of Transaminase Determinations during an Intrahospital Epidemic.** *Amer. J. Med. Sci.* 1961, Apr., v. 241, No. 4, 454–8, 1 fig.

After a minor outbreak of infectious hepatitis among staff and patients at the University of Kansas Medical Centre, blood samples from staff were examined for serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamic-pyruvic transaminase (SGPT) activity. Of 193 samples examined, 4 showed levels above normal: one was from a nurse recovering from infectious mononucleosis, 2 were from personnel with no evidence of hepatitis, and 1 was from a student admitted to hospital 1 week later with hepatitis. Another patient had a normal SGPT level in the early stages of her illness but 5 days later had a level of 2,500 units. After gamma globulin was given to staff in the dose of 0·01 ml. per lb. body weight no further cases of infectious hepatitis occurred. *A. B. Christie*

ALEINIK, M. D. & TARANIUK, Z. E. **The Heterohaemagglutination Test with Chick Red Cells as a Method for the Laboratory Diagnosis of Infective Hepatitis.** *Problems of Virology.* London. 1960, v. 5, No. 1, 89–93, 1 fig. [Translated from Russian.]

The authors have investigated the titres of agglutinins for chick red cells in the sera of 417 patients suffering from infective hepatitis and of 187 healthy persons and patients suffering from other diseases. In preliminary experiments it was found that different titres were obtained with cells from different birds, and it

was therefore necessary to select a bird with cells giving a high titre before beginning the main investigation, which was carried out with a 0·5% suspension of red cells, the result being read after 18 hours at 4°C. A titre of 5 or higher was observed in 265 patients with infective hepatitis (63·5%) and in 22 persons in the control group (11·8%). The frequency of positive results was not related to the severity of the disease or to the results of the aldolase test. *D. J. Bauer*

WEINBACH, R. O nouă reacție serologică pentru recunoasterea hepatitei virotice: aglutinarea hematiilor formolate si tante de om (aglutinarea-HFT). [**A New Reaction for recognizing Infective Hepatitis: the Agglutination of Tannin-Treated Formolized Human Erythrocytes (TFE-Agglutination)**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, Nov.–Dec., v. 5, No. 6, 565–7.

The author has observed that human red cells which have been formolized and treated with tannic acid are agglutinated by certain sera, in particular by the sera of patients suffering from infective hepatitis, and the effect has been used as the basis of a test for diagnosing this condition. A suspension of formolized group O red cells in distilled water containing 10^6 cells per cmm. is mixed with an equal volume of 0·01% tannic acid solution in saline buffered with 0·15 M *p*H 7·2 phosphate buffer and incubated at 37°C for 30 minutes. The cells are then washed and made up in buffer with 0·005% thiomersal as a 10% suspension which can be stored at 4°C. for 2 years or longer. For carrying out the test the suspension is diluted 1 in 5 or 1 in 10 with a diluent consisting of 0·5% polyvinylpyrrolidone in buffer. Serial 2-fold dilutions of the test serum are prepared and mixed with the red cell suspension; the test may be carried out in wells in a rotating plate, when the results are read after 45 minutes at room temperature, or in tubes, which are kept at 4°C. for 2 hours or longer. *D. J. Bauer*

STÖCKER, E. M. Über morphologische Leberveränderungen mit Hepatitisvirus beimpfter Hühnerembryonen. [**Morphological Changes in the Livers of Chick Embryos infected with Hepatitis Virus**] *Arch. f. Hyg. u. Bakt.* 1960, Oct., v. 144, No. 7, 535–49, 14 figs. [36 refs.]

An investigation has been made of the histopathology of the liver in several thousand chick embryos infected by various routes with material from patients suffering from infective hepatitis, and with control materials containing other infectious agents. Lesions which were considered to be specific for infective hepatitis infection were observed in a proportion of cases [which is not clearly stated]; the liver was brownish-yellow or green, and its blood vessels were dilated and contained necrotic red cells, many monocytes and histiocytes. The cells also surrounded the vessels and invaded the liver parenchyma, which showed a corresponding degree of damage in the form of vacuolation of the nuclei leading to karyorrhexis and karyolysis, and vacuolation of the cytoplasm leading to disruption of the cell. These appearances are illustrated in photomicrographs. Lesions could sometimes be seen in the liver of embryos which had been injected with sodium chloride solution, but they could be distinguished from the specific changes by their predominantly autolytic character. *D. J. Bauer*

ANDERSON, S. G., DOHERTY, R. L. & CARLEY, J. G., with the technical assistance of Margaret MCELROY & Patricia TREVETHAN. **Epidemic Polyarthritis: Antibody to a Group A Arthropod-Borne Virus in Australia and the Island of New Guinea.** *Med. J. Australia.* 1961, Feb. 25, v. 1, No. 8, 273–6, 1 fig. [11 refs.]

10 major epidemics of polyarthritis have occurred in Australia and islands to the north since 1928. One in the Murray Valley in 1956 was shown to be probably due to a group A arthropod-borne virus related to the Malayan AMM 2354 virus. Human sera from various areas were tested in a suckling-mouse neutralization test against AMM 2354 [this *Bulletin*, 1960, v. 35, 679]. Of samples of 7–121 sera from 9 areas of Queensland 7–81% had antibody. Antibody was found also in 22% of 23 sera from the north of Northern Territory, in 33–100% of 3 groups of 15–24 sera from coastal Papua and New Guinea, in 29% of 85 from the Murray Valley and in 19% of 36 from Western Victoria. No antibody was found in the sera of 40 children from the New Guinea Highlands and only in 3 of 117 sera from southern Victoria. Of domestic animal sera from Queensland 48 of 66 horses, 12 of 40 cattle and 4 of 7 pigs had antibody. Low titre antibody was also found in wild mice, in 1 of 30 sheep and in 2 of 7 possums (*Trichosurus vulpecula*) but the significance of these is doubted. No antibody was found in 8 goats, 11 dogs, 19 cats, 10 water-rats, 12 *Rattus rattus*, 10 *R. norvegicus* and 38 bandicoots. Only 2 sera from domestic and wild birds from various infected areas had antibody; a night heron (*Nycticorax caledonicus*) and a duck of unknown species, the latter in low titre. The antibody detected appears to be due to infection with 1 or more group A viruses not yet isolated. *C. E. Gordon Smith*

DOHERTY, R. L., ANDERSON, S. G., AARON, K., FARNWORTH, J. K., KNYVETT, A. F. & NIMMO, D. **Clinical Manifestations of Infection with Group A Arthropod-Borne Viruses in Queensland.** *Med. J. Australia.* 1961, Feb. 25, v. 1, No. 8, 276–9.

Sera from 12 patients suffering from illnesses with arthralgia or rash in Queensland between 1958 and 1960 were tested for antibody to AMM 2354—a Malayan mosquito virus in group A. 2–3 specimens of serum from each patient were tested for complement-fixing and neutralizing antibody—the first specimens were 6–20 days and the second 22–315 days after onset. 1 patient, 43 years old, had a diagnostic rise in complement-fixing and neutralizing antibody—he had a febrile

illness which started with aching legs and a painful heel followed by a maculopapular rash on the trunk, arms and face with an area of confluent macules on the right shin. The rash lasted 4 days but 3 days later he had a short episode of headache, malaise and muscle pains. 3 patients in a family whose first sera were collected late had either a falling antibody level or stationary neutralizing antibody with a rise in complement-fixing antibody. All had polyarthritis, one a rash and two of them electrocardiographic evidence suggestive of myocarditis. Significant rises in both types of antibody were found in a boy aged 6 with fever but neither arthritis nor rash. The tests on the other 8 patients did not suggest that the illnesses had been due to infection with a group A virus although 5 of them had neutralizing antibody presumably due to a previous infection. *C. E. Gordon Smith*

SPENCE, L., BELLE, E. A., MCWATT, E. M., DOWNS, W. G. & AITKEN, T. H. G. **An Outbreak of Equine Encephalitis in the Rupununi, British Guiana.** *Amer. J. Hyg.* 1961, Mar., v. 73, No. 2, 173–81, 1 fig. [19 refs.]

"The virus of eastern equine encephalitis has been shown to be responsible for an epizootic in horses in the Rupununi Savannah, British Guiana. Neutralizing antibodies to both eastern and western equine encephalitis viruses were encountered in equines. Both EEE and WEE were isolated from the brain of a single horse."

GORALSKI, H. Une epidémie d'encéphalite à tiques en Pologne. **[Encephalitis in Poland]** *World Neurology.* Minneapolis. 1961, Apr., v. 2, No. 4, 336–42, 3 figs.

The English summary appended to the paper is as follows:—

"Foci of tick-borne encephalitis have been observed in Poland in the vicinity of Nysa in Lower Silesia (1950), in the province of Bialystok, near the great forest of Bialowieza (1954), and in the province of Olsztyn (Mazury) in 1954.

"This last epidemic occurred mostly in the summer months (June to October) in humid areas of rich, green forests. In the neurologic service at Olsztyn 35 cases were observed; diagnosis was verified by serologic and virologic studies in 13 cases. Duration of the illness was approximately 109 days. Most of the patients were forestry labourers and peasants of 20 to 50 years of age. In 4 cases, persistent neurologic symptoms remained and 1 case ended in death. In 4 cases, the temperature curve was biphasic. The following clinical symptoms were noted: meningeal, 4 cases; cerebral, 4 cases; spinal, 1 case; polyradiculitis, 1 case; mixed, 3 cases.

"The tick responsible for this epidemic appeared to be the species *Ixodes ricinus* (common tick or 'dog tick')."

VAN TONGEREN, H. A. E. & TIMMERS, W. C. **Antibody Studies in Coots (Fulica atra) to Russian Spring-Summer Encephalitis (CEE) Virus in the Netherlands. The Behaviour of this Virus in Experimentally Inoculated Coots.** *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 5, 606–16, 1 fig. [20 refs.]

Sera from 156 coots (*Fulica atra*) were collected in February/March 1960 in north Holland. 135 single sera and 8 pools comprising 21 sera were tested in an intraperitoneal neutralization test against the Graz I strain of Central European tick-borne encephalitis virus. 10 single sera were found to have neutralizing indices of 175 to over 100,000. However, most of these positive sera were markedly haemolysed and some at least were contaminated with fluid from the gizzard as the blood was collected by decapitation. Gizzard fluid was shown to be capable of neutralizing 10,000 LD50 of virus so that little significance can be attributed to these antibody studies.

All the coots were infested with the mite *Pseudomenopon pilosum,* and 3 other species were found less frequently.

4 coots which survived shooting were given about 10,000 LD50 of virus subcutaneously. 1 died of its injuries on the 3rd day: virus was recovered from the blood and liver (about 7,000 LD50 per ml. or gm. respectively) and from spleen and kidney (about 1,000 LD50 per gm.). The remaining 3 circulated virus from the 2nd to the 8th or 10th day with maximum titres of 1,000–5,500 LD50 per ml. on the 4th to 6th days. 2 of them had high neutralizing antibody titres by the 17th day while the 3rd had antibody at death on the 29th day. It died of progressive weakness and a low titre of virus was isolated from the brain (50 LD50 per ml.) but not from blood, liver, spleen or kidneys. Mites from the experimentally infected coots were also examined for virus but none found. It is not known whether the species found feed on blood or tissue fluid. *C. E. Gordon Smith*

DUBOV, A. V. **Virological Diagnosis of Tick-Borne Encephalitis by the Tissue Culture Method.** *Problems of Virology.* London. 1960, v. 5, No. 4, 447–51, 2 figs. [Translated from Russian.]

Blood samples were collected from 76 patients with tick-borne encephalitis—mainly of the meningeal type. The blood-clot was covered with 50% glycerol and later washed and ground up before inoculation of cultures. Cultures of trypsinized human embryo skin-muscle were used. 8 blood samples collected 2–8 days after the onset of illness caused cytopathic changes in the cultures after 1–3 passages. These strains failed to cause cytopathic changes in HeLa cells even after passage. They were identified as tick-borne encephalitis virus by neutralization tests. [At least one of these appears to be of doubtful significance.]

Neutralization tests were carried out with the Sofin strain of virus on paired sera from 60 patients. A 2-fold [*sic*] or greater rise in titre was demonstrated in 36, similar titres in both sera in 15, and both sera were negative in 9. *C. E. Gordon Smith*

WILLIAMS, M. C. & WOODALL, J. P. **O'Nyong-Nyong Fever: an Epidemic Virus Disease in East Africa. II. Isolation and some Properties of the Virus.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1961, v. 55, No. 2, 135–41, 1 fig. on pl.

In June 1959, 7 acute-phase blood samples from patients with O'Nyong-Nyong fever [this *Bulletin*, 1961, v. 36, 380] were inoculated into suckling and adult mice. Some suckling mice showed retarded growth, paralysis and patchy alopecia but in spite of 5 passages in suckling mice no virus was isolated. Of 11 convalescent sera 9 had at least 2 log neutralizing antibody to Chikungunya, 2 to Semliki Forest and 1 to Sindbis viruses. An acute phase serum in July was inoculated undiluted and diluted 10^{-1} and 10^{-2} into 1-day suckling mice. After 3 passages a virus was isolated from the diluted lines. Retardation of growth and patchy alopecia were noted in early passage. The agent passed a Seitz filter. On passage a titre of 6 log was attained by intracerebral inoculation of 2-day mice but 35–42 day mice were unaffected. The virus was re-isolated and cross-neutralization established its identity with the isolate. The patient's serum showed an increase in neutralizing index from 0·1 to 3·6 between the 1st and 11th days of disease. At least 4 log of the virus were neutralized by Chikungunya antiserum. Its titre was reduced 2 log by ether at 4°C. overnight. Acetone-ether and sucrose-acetone extraction of mouse-brain gave a haemagglutinin active at *p*H 7·3–7·4 but it was unstable. At least 15 apparently similar agents have been isolated from human sera and mosquitoes.

J. S. PORTERFIELD studied one of these isolated from *Anopheles* (*Myzomyia*) *gambiae* after 5 passages in 1-day mice. This produced plaques in 48 hours on chick embryo fibroblast monolayers. The maximum size of the plaques was 5–10 mm. on the 6th day. Plaque inhibition [*ibid.*, 1960, v. 35, 715] by a variety of antisera showed that it was inhibited by the homologous antiserum and by Chikungunya and Semliki antisera. O'Nyong-Nyong antiserum failed however to inhibit Chikungunya or Semliki plaques.

The patchy alopecia is considered an important sign of infection with early passage virus. It appears 4–9 days after inoculation in the hair of the sides, back or head, or at the base of the tail. If the mice do not sicken the hair may return by the 11th or 12th day after inoculation. More than 15 passages, alopecia being used as the indicator, may be necessary to establish a strain of O'Nyong-Nyong virus.

C. E. Gordon Smith

SOLANO S., L. E., COTO C., R. A. & ASTORGA A., Julieta. Observaciones sobre mononucleosis infecciosa. **[Observations on Infectious Mononucleosis]** *Acta Méd. Costarricense.* 1960, Sept.–Dec., v. 3, No. 3, 245–53. [13 refs.] English summary.

The Paul Bunnell test, differential white cell count, and liver function tests were carried out on 100 patients suspected clinically of suffering from infectious mononucleosis. The Paul Bunnell test was regarded as negative if agglutination was absent in dilutions over 1 in 56, doubtful between 1 in 56 and 1 in 112, and positive only if present over 1 in 112. On this basis, 38 were negative, 22 doubtful and 40 positive: only 50% of the patients with positive reactions showed typical changes in the differential white cell count. In only 4 patients was the thymol flocculation test positive but the cephalin cholesterol test (Hanger) was strongly positive in 50 patients, and negative in only 40. The authors conclude that the Paul Bunnell test can be regarded only as presumptive diagnostic evidence and that the Hanger test is too sensitive. *A. B. Christie*

ROJNIK, A. Primer spontane rupture vranice pri infektivni monunokleozi. **[Spontaneous Rupture of Spleen in Infectious Mononucleosis]** *Zdravstveni Vestnik.* Ljubljana. 1960, v. 29, Nos. 11/12, 356–8, 4 figs. German summary.

KITCHEN, W. H., JACK, I. & GORRIE, C. J. R. **Granuloma from Scabby Mouth Virus.** *Med. J. Australia.* 1961, Mar. 4, v. 1, No. 9, 322–4, 1 fig. [18 refs.]

Orf, contagious pustular dermatitis, ecthyma contagiosum, and scabby mouth are the names given to a disease of sheep and of goats, caused by a dermotropic virus of world wide distribution [this *Bulletin*, 1956, v. 31, 401; 1957, v. 32, 855]. Vesiculo-pustular lesions occur on the lips, muzzle and other non-wool-bearing skin areas. Human infections have been recognized in those handling infected animals, and in laboratory workers. A case report of the disease in a 3-year-old child in Melbourne is recorded. Infection was probably derived from a pet lamb and the child had a granulomatous lesion on the left deltoid region. A trivial burn complicated the clinical picture; the auxiliary nodes were enlarged and tender and there was a rise in temperature. A description of the appearance of the biopsy specimen is given and the identity of the infective agent was confirmed on the basis of the production of an erythematous lesion on the thigh of a lamb with a centrifugate of a suspension of the specimen; a similar lesion was produced with the standard vaccine strain of this virus. Antibiotic therapy probably reduced the effect of a secondary infection with staphylococci and the underlying virus disease subsided spontaneously.

This record adds another example of the possible infections conveyed to children by pets in the home [this *Bulletin*, 1959, v. 34, 128]. *R. Lovell*

CROME, L. **Cytomegalic Inclusion-Body Disease.** *World Neurology.* Minneapolis. 1961, May, v. 2, No. 5, 447–58, 7 figs. [30 refs.]

A review with a report of a case.

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; Colicines; other Therapeutic Substances; Disinfection**

LINTON, A. H. **Interpreting Antibiotic Sensitivity Tests.** *J. Med. Lab. Technol.* 1961, Jan., v. 18, No. 1, 1–20, 8 graphs, 2 pls. & 1 fig. [22 refs.]

The author first refers to a recent collaborative study [TILL *et al.*, this *Bulletin*, 1961, v. 36, 172] which showed that different workers could obtain widely divergent results in testing the sensitivity of the same organisms to antibiotics. He then goes on to a detailed analysis of the effect of different factors on the width of inhibition zones produced in an agar diffusion test. In simple terms (not used by the author) this is determined in the first place by a race between antibiotic diffusion and bacterial growth: slowly growing organisms will show correspondingly wide zones, and if growth is delayed by a slow rise to incubator temperature there will be a similar effect. In this connexion a graph shows the lag in temperature rise in a plate in the middle of a pile surrounded by others. Particulars are also given of the effect of temperature on the rate of diffusion of some antibiotics.

Inoculum size is an important factor: 2 full-page photographic illustrations show this, the example chosen being streptomycin [which is in fact more affected by this than any other common antibiotic: that penicillin, for instance, is much less affected in most tests is not mentioned, although reference is made to the special problem of testing penicillinase-forming staphylococci]. The medium may affect the result, both in the sense that its ordinary constituents may reduce the activity of some antibiotics, and according to its *p*H. The depth of the medium is important if discs are used. The time of diffusion before incubation begins should be constant: deliberate pre-diffusion is advised only for antibiotics of large molecular size, such as polymyxin. Finally, the mode of application of the antibiotic must be considered, whether as a solution in a cup or cylinder, or to the surface in a disc or tablet. Desirable concentrations or quantities are not specified: these depend in part on another factor considered, the different rates of diffusion of different antibiotics.

The paper concludes with a section on the practical conduct of sensitivity tests, defining their aims, describing diffusion methods for both primary and pure cultures, and the controls advisable: *i.e.* the inclusion of a standard organism of known sensitivity, and verification of the potency of the antibiotics used, particularly if in the form of discs. A rather unusual method is described for more accurate determinations, and the paper concludes with some advice on the terms of reporting results. *L. P. Garrod*

WALLMARK, G. & FINLAND, M. **Comparative Activity of Various Penicillins against Penicillinase-Producing and Nonpenicillinase-Producing Staphylococci.** *Proc. Soc. Exper. Biol. & Med.* 1961, Jan., v. 106, No. 1, 78–85, 3 figs. [15 refs.]

The authors compared the activities of 7 different penicillins on a number of strains of staphylococci. Considerable differences were observed, details of which must be sought in the original. Some penicillins, such as benzyl and phenoxy methyl, showed little difference in *in vitro* activity against producers or non-producers of penicillinase, regardless of inoculum. The phenethicillins were more active than, for example, benzyl against penicillinase-producers when the inoculum was large but not when it was small. Dimethoxypenicillin was especially active against large inocula of penicillinase-producers but less active than the others against small inocula or against non-penicillinase producing strains. *R. E. O. Williams*

STEINMAN, H. G. **A Biochemical Comparison of 6-Aminopenicillanic Acid, Benzylpenicillin, and 2,6-Dimethoxyphenylpenicillin.** *Proc. Soc. Exper. Biol. & Med.* 1961, Jan., v. 106, No. 1, 227–31, 3 figs. [14 refs.]

This author reports observations which confirm and to some extent amplify those of others. He first examined the susceptibility of benzyl penicillin (G), methicillin (DMP) and 6-aminopenicillanic acid (6-APA) to 2 penicillinases: denoting the rate of hydrolysis of G as 100, those of DMP and 6-APA by *Bacillus cereus* penicillinase were 1·6 and 0·8 respectively and those by *Staphylococcus aureus* penicillinase were 0·35 and 0·1. He also studied the induction of penicillinase

formation by the 3 compounds: DMP was the most effective inducer in both *B. cereus* and *Staph. aureus*. G and 6-APA were more active inducers for the former than for the latter. A penicillinase-forming strain of *Staph. aureus* underwent a 170-fold increase in resistance to DMP in 6 transfers in the presence of this substance, but the change did not appear to be due to increased enzyme formation. *L. P. Garrod*

ROBERTS, C. E., Jr., ALLEN, J. D. & KIRBY, W. M. M. **Laboratory and Clinical Studies of Penicillin X-1497.** *Clin. Pharmacol. & Therap.* St. Louis. 1961, Jan.–Feb., v. 2, No. 1, 70–79, 4 figs. [10 refs.]

This is an account of the authors' first experiences, both laboratory and clinical, with the form of penicillin now known officially as methicillin [this *Bulletin*, 1961, v. 36, 173, 174, 175]. *In vitro* tests showed its lesser activity against streptococci and pneumococci, and its uniform activity in a concentration of 2 or 5 μgm./ml. against staphylococci regardless of high resistance to penicillin G. It was shown also to have a bactericidal and a lytic action on staphylococci, the former being compared with those of vancomycin and bacitracin, both of which were inferior to the extent that regrowth was more liable to occur after the earlier fall in the viable count. Staphylococci exposed to methicillin became resistant at about the same rate as to penicillin G: in parallel experiments with vancomycin little resistance developed. Observations were also made on its stability. The clinical studies included estimations of the levels attained in the blood of patients, which were shown to be raised by also giving probenecid, and administration to 23 patients, 11 of whom had various staphylococcal infections, 9 of whom were "improved", 9 had various pulmonary infections, 7 of which were "cured", 2 streptococcal cellulitis, both cured, and 1 cat scratch disease (unimproved). Side effects were negligible. [The authors themselves would presumably not wish much importance to be attached to these briefly reported clinical findings: in particular the "cure" of streptococcal and "probable pneumococcal" infections when staphylococcal were only improved, does not indicate the relative value of this drug in these types of infection.] *L. P. Garrod*

PFALTZ, C. R., HERZOG, H., STAUB, H. & WEY, W. Zur ototoxischen Wirkung hoher Streptomycindosen. [**The Ototoxic Action of High Streptomycin Dosage**] *Schweiz. med. Woch.* 1960, Dec. 17, v. 90, No. 51, 1472–8, 6 figs. [Numerous refs.]

This is a collaborative study by physicans and otologists at Basel. Pulmonary tuberculosis in 211 patients was treated by continuous intravenous infusion of 3 drugs for an average period of 5 weeks: these were dihydrostreptomycin pantothenate, of which most patients had 2 gm. daily but some 1 or 3 gm., 24 gm. PAS and 5–10 mgm./kgm. isoniazid. The object of continuous infusion was to prevent the attainment at any time of unduly high streptomycin blood levels, and numerous assays showed blood levels averaging about 5, 10 and 15 μgm./ml. for the 3 doses used, although with rather wide variations. Frequent tests of the function of both branches of the 8th nerve were carried out during and after treatment.

Vestibular function was found to be impaired in 17% of patients before treatment began: 4% developed reversible impairment during treatment, and 4% sustained irreversible damage. Hearing was impaired in 47% of patients before treatment was begun: 1·5% had temporary impairment (hearing loss in the high frequency range) during treatment, and 10 cases (5%) suffered permanent damage: 5 of these had had some impairment before treatment. The danger of serious damage is greater in patients with some original impairment of function: periodic tests should be done and serious consideration given to stopping treatment if there are early signs of further damage. Analysis of the findings showed that the frequency of 8th nerve damage was unrelated to either the daily or the total dose given, and unrelated to age (both of which conclusions are surprising) but was clearly correlated with impairment of renal function. The authors are satisfied that the combination with pantothenic acid and their system of continuous administration both diminish the risk.

L. P. Garrod

SGARZI, B., LUGLI, Anna M. & GIOLITTI, G. **An Antibiotic Complex from Streptomyces, No. 1415.** *Antibiotics & Chemotherapy.* New York. 1961, Feb., v. 11, No. 2, 97–102, 4 figs.

An antibiotic complex of low toxicity produced by a Streptomyces is described. It is active against some Gram-positive bacteria resistant to certain other antibiotics.

HABERMANN, V. **The Effect of 6-Azauracil on Microorganisms inhibited by Chloramphenicol.** *Biochim. et Biophys. Acta.* 1961, Apr. 29, v. 49, No. 1, 204–11, 3 figs. & 1 diagram. [18 refs.]

KUNIN, C. M. & FINLAND, M. **Clinical Pharmacology of the Tetracycline Antibiotics.** *Clin. Pharmacol. & Therap.* St. Louis. 1961, Jan.–Feb., v. 2, No. 1, 51–69, 3 figs. [121 refs.]

This is a comprehensive and well documented review of the literature on tetracycline and chlor-, oxy- and demethylchlortetracycline, so far as it concerns their pharmacological behaviour. Data on levels attained in the blood are presented both in w/v terms and in terms of the activity of the serum against a particular organism, with a preference for the latter method of expression. The mechanism of absorption from the alimentary tract is discussed, together with factors interfering with or promoting it. In connexion with studies on distribution in the body, work is described which shows that tetracyclines are deposited in growing bone and in tumours. Protein binding, biliary excretion and renal excretion are dealt with, and there is finally a full discussion of "toxic" effects, notably

those based on changes caused in the intestinal flora. Although differences in the pharmacological behaviour of the 4 drugs are pointed out, no attempt is made to distinguish between their therapeutic merits.

L. P. Garrod

YOW, Martha D. & TENGG, N. E. **The use of Kanamycin Sulfate as a Therapeutic Agent for Infants and Children. An Analysis of 140 Cases treated during a Two-Year Period.** *J. Pediatrics.* St. Louis. 1961, Apr., v. 58, No. 4, 538–47, 2 figs. [13 refs.]

In 2 years, the authors treated 140 infants and children with kanamycin, the dose finally employed being 12·5 to 50 mgm. per kgm. daily: 78 infections were due to *Staphylococcus aureus*, 28 to *Escherichia coli*, 5 to *Klebsiella pneumoniae*, 5 to *Proteus* species and 1 to streptococci: in 23 cases the type of infection was not established. The drug is usually given intramuscularly and is rapidly absorbed; when given by mouth absorption is irregular, but it can be given for gastro-intestinal infections. The drug is bactericidal and it may be effective against staphylococci resistant to other antibiotics. It is nephrotoxic and ototoxic; there was no evidence of nephrotoxicity in this series, auditory studies of 50 treated children are still in progress.

A. B. Christie

GERKE, J. R. & MADIGAN, Mary E. **Amphotericin B and other Polyene Antifungal Antibiotics: Photometric Assay and Factors influencing Activity.** *Antibiotics & Chemotherapy.* New York. 1961, Apr., v. 11, No. 4, 227–37, 3 figs.

LEE, C. C. & FROMAN, R. O. **Passage of Erythromycin into the Aqueous Humor.** *Antibiotics & Chemotherapy.* New York. 1961, Feb., v. 11, No. 2, 107–9.

Rapidity of the passage of propionyl erythromycin vs. erythromycin base into the aqueous humor is shown.

SOKOLSKI, W. T., BURCH, M. R. & WHITFIELD, G. B. **A Microbiological Assay for Endomycin in the Presence of Neomycin.** *Antibiotics & Chemotherapy.* New York. 1961, Feb., v. 11, No. 2, 103–6, 1 fig.

GRÄF, W. & BICKEL, H. Antibiotische Eigenschaften und Toxizität des Wirkstoffes aus *Pseudomonas fluorescens.* **[Antibiotic Properties and Toxicity of the Active Substance from *Pseudomonas fluorescens*]** *Arch. f. Hyg. u. Bakt.* 1961, Feb., v. 145, No. 1, 21–31, 6 figs.

The extraction of an antibiotic, the subject of this paper, from *Pseudomonas fluorescens* has already been reported by the senior author and his colleagues. It is distinct from any substance formed by *Ps. pyocyanea.* It has apparently been obtained in a pure state, and is said to be a polypeptide coupled to an organic acid. Its sodium salt was used in these experiments, the substance itself being poorly soluble. It has a lytic action on amoebae, but not on their cysts, in concentrations of 0·01% or less, and similar effects were demonstrated on *Trichomonas vaginalis, Leishmania donovani* and *Trypanosoma brucei.* Among bacteria, various Gram-negative species, staphylococci and *Streptococcus faecalis* were unaffected, but *Strep. pyogenes*, pneumococci and *Corynebacterium diphtheria* were inhibited by 0·01% or less.

A somewhat unconvincing experiment is described in which application of the substance to the mouths of mice caused alpha-haemolytic streptococci to disappear. Addition to a suspension of influenza virus caused a fall in haemagglutinin titre and lysis of virus particles as revealed by electron microscopy (this and some disintegrating amoebae are illustrated), but there was no action on vaccinia virus or bacteriophage. Some pathogenic fungi were also unaffected. The substance is strongly haemolytic, and toxic when injected intraperitoneally in mice (LD50 66 mgm./kgm.) but harmless when given orally. Since none could be detected in the faeces it is assumed to be destroyed in the stomach, and will therefore not serve for the treatment of amoebic dysentery, but the authors are hopeful that some local therapeutic uses may be found for it, including the treatment of *T. vaginalis* infection. *L. P. Garrod*

J. PHARMACY & PHARMACOL. London. 1960, Dec., v. 12, Suppl., 9T–40T, 6 figs. [72 refs.] **Symposium on Chemical Disinfection.**

The following 3 papers were the principal contributions to a symposium at the British Pharmaceutical Conference, 1960: there is no further report of the proceedings except a much condensed account of a miscellaneous discussion.

S. E. JACOBS. *Some Aspects of the Dynamics of Disinfection* (pp. 9–18). The author briefly reviews the earlier elaborate studies by JORDAN and himself [this *Bulletin*, 1946, v. 21, 260, 538 *bis*] of the action of phenol on *Escherichia coli*, many of these experiments being carried out with a large volume of aerated medium from which aliquots were removed at intervals and replaced with fresh medium, in order to maintain a constant population. Here he gives a preliminary account of further experiments by the same method designed to determine the "threshold concentration" of phenol for this species at 35°C.,—*i.e.* the minimum concentration which will achieve "virtual sterilization". Some of these experiments were continued for as long as 10 days, and some anomolous results were obtained, the reasons for which are discussed.

A. M. COOK. *Phenolic Disinfectants* (pp. 19–28). This is a condensed review of a large subject, dealing with mode of action, test methods, and factors affecting activity. Much attention is devoted to the effect of soaps on the activity of phenols, an important consideration in formulating a lysol. There follows an account of the different types of tar acid obtained by

distillation and their method of formulation to obtain such products as "white" and "black" fluids, and a brief indication of suitable spheres of use.

J. G. Davis. *Chemical Sterilization* (pp. 29–39). This is a general discussion on an even wider subject, most of which is covered by the definition "the application of germicides in industry." Emphasis is placed on the importance of cleaning as well as exerting antibacterial action, and the first table gives methods for cleaning and "sterilizing" pipe-lines, tanks, cans and bottles: another compares the advantages and draw-backs for such purposes of heat, chlorine and "quats". The properties of these and other appropriate germicides (alkalis, iodophors, chlor-phenols and ampholytic compounds) are defined; there are remarks on the effect of organic matter, the nature of surfaces to be sterilized, and the dangers of corrosion, and finally some on application to dairying, brewing, catering, laundering and other industries. *L. P. Garrod*

Kundsin, Ruth B. & Walter, C. W. **In-Use Testing of Bactericidal Agents in Hospitals.** *Applied Microbiol.* Baltimore. 1961, Mar., v. 9, No. 2, 167–70.

The authors consider that the valid test of germicidal products or processes is their bacteriological evaluation under the actual conditions of use. This paper describes the results of some such tests. The efficiency of various detergent disinfectant solutions for floor cleaning was compared over a six-month period by the use of floor counts. A synthetic phenolic disinfectant gave consistently lower bacterial counts than an iodophor or quaternary ammonium salts in the concentrations used, although the differences were not striking. Germicidal floor waxes were only of value in that they did not become contaminated during storage.

A few counts on fluids from laundry processes showed the value of an unspecified germicide in the final rinse. Another experiment reported only in outline showed an accelerated die-away of added staphylococci from cloth which had been treated with an unspecified germicide.

Finally, figures are given for a room in actual use by patients with walls, floors and fittings cleaned by a germicidal spray, the floor washed with germicide, the bedding sterilized by ethylene oxide, ventilation controlled by the admission of only filtered air and an ultra-violet "curtain" at the door. The average number of airborne organisms was 1·5 per cu. ft. The average air fall-out was 3·5 organisms per sq. ft. per minute, and the average floor count was 2·6 organisms per sq. cm. Similar results can be obtained in operating rooms. The experience of 4 years has shown that air counts of 20 organisms per cu. ft. and fall-outs of 20 organisms per sq. ft. per minute can be obtained without artificial ventilation by the use of disinfectant washing and careful techniques.

The authors conclude that the bacterial population of a hospital is the difference between the numbers introduced by patients, personnel and air currents and the number removed by ventilation and cleaning procedures. Properly used, germicides reduce bacterial counts in the air and on surfaces. To ensure that hygienic measures are efficiently carried out, and to evaluate new procedures, regular bacteriological monitoring is indispensable. *J. C. Kelsey*

Mitsuhashi, S., Harada, K. & Kameda, M. **Elimination of Transmissible Drug-Resistance by Treatment with Acriflavin.** [Correspondence.] *Nature.* 1961, Mar. 18, v. 189, 947. [14 refs.]

These authors, from Gunma University, Japan, have previously reported the isolation from cases of epidemic dysentery of strains of *Shigella flexneri* and *Escherichia coli* resistant to sulphanilamide, streptomycin chloramphenicol and tetracycline. They also refer to the work of other Japanese authors who claim to have transmitted this multiple resistance from one to the other of these species by cultivating them together. Here they report that this transmissible drug-resistance can be abolished by cultivating in broth overnight in "sub-lethal" concentrations of acriflavine (10 and 20 μgm./ml. respectively for the 2 species). These cultures were plated and numerous colonies tested: about 2% of *E. coli* and 40% of *Sh. flexneri* reverted to (apparently full) drug-sensitivity in 2 of 3 strains of each organism, the 3rd of each remaining unaffected. *L. P. Garrod*

Burn, J. I. & Coleman, S. J. **Clinical and Bacteriological Evaluation of Furaltadone (Altafur).** *Antibiotic Med.* New York. 1961, Jan., v. 8, No. 1, 37–44.

This paper is from the Postgraduate Medical School of London (Hammersmith Hospital) and reports the results of giving furaltadone (Altafur) to 40 patients in surgical wards. Only the oral form of this drug was available, and the usual dose given was 500 mgm. followed by 250 mgm. at 6-hour intervals. Blood assays were done in 9 patients after the initial dose: after 2 hours the concentration found was 6·2 or 3·1 (in 1 instance 12·5) μgm./ml.: after 5 hours it was usually 3·1 μgm./ml. The susceptibility to the drug of the bacteria from the patients was determined by the ditch plate method with a standard staphylococcus for comparison: all strains of staphylococci and pneumococci were sensitive, but only 4 of 11 of *Escherichia coli,* and none of *Pseudomonas pyocyanea* or *Proteus.*

In general the clinical results were judged to be favourable; 29 of the 40 patients were improved and 11 of these were cured. The outcome was determined in part by the nature of the infection, those due to the resistant species referred to above naturally faring badly. The conditions treated fell into 3 classes; respiratory infections (pneumonia or acute bronchitis mostly due to pneumococci) with 10 cases, all improved, urinary tract infections, with 11 cases, 5 improved, 5 unaffected and 1 doubtful, and 19 cases of wound infection and other forms of local sepsis, caused by staphylococci and various other bacteria, with 14 improved, 1 unaffected and 4 doubtful. Side

effects were limited to nausea and occasional vomiting. No cases of blood stream infection were treated. As the authors admit, this was not a controlled trial, and they can give only their "over-all impression" of the worth of this drug. *L. P. Garrod*

BUZARD, J. A. & CONKLIN, J. D. **The Distribution of Furaltadone in the Rat.** *Antibiotics & Chemotherapy.* New York. 1961, Feb., v. 11, No. 2, 89–96, 5 figs. [13 refs.]

Furaltadone is rapidly absorbed from the small intestine and colon and is widely distributed in the body after absorption.

UNDERWOOD, G. E. & WEED, S. D. **The Effect of Carbonyl Compounds on Poliovirus.** *Virology.* New York. 1961, Jan., v. 13, No. 1, 138–9.

Glyoxal and a higher member of the series Kethoxal (β-ethoxy-α-ketobutyraldehyde hydrate) were found to be efficient viral inactivating agents [this *Bulletin*, 1957, v. 32, 1092]. Various doses of these substances were compared with formaldehyde in their effect on viruses after 4 hours at 37°C. In general, Kethoxal was similar in activity to formalin against many viruses and so was glyoxal where tested. However, both glyoxal and Kethoxal were without effect on an attenuated strain of type 2 poliovirus (Kethoxal was also tested and found ineffective against the MEF 1 strain). Viruses that were inactivated included vaccinia, Newcastle disease, influenza A and B, mumps, measles, herpes simplex, Western equine encephalitis, adeno viruses, mouse hepatitis and some unspecified "recently isolated respiratory viruses". On the basis of the observed differential inactivating effect the authors suggest that glyoxal or Kethoxal might prove valuable for removing viruses from attenuated poliovaccine. *A. J. Beale*

v. WASIELEWSKI, E. & KOBERG, W. Experimentelle Untersuchungen zur thermischen Desinfektion virusinfizierten Waschgutes. [**Experimental Studies of the Heat Disinfection of Virus-infected Linen**] *Arch. f. Hyg. u. Bakt.* 1961, Feb., v. 145, No. 1, 44–60, 9 figs. [49 refs.]

This paper describes a laborious study of the effect of washing processes on soiled linen and secondly on viruses contained in such material. Pieces of linen were soaked in guineapig blood, dried, rubbed with sand paper to remove any excessive thickness of dried blood and then immersed in water containing simple soap powder or proprietary German soaps or cleansing agents (composition undisclosed) and heated first to 40° and then to 80°C. for specified times. Total nitrogen estimations were then made of the material and of the fluid in which they had been treated to determine how much blood had been extracted. In another series of such tests amino acids were estimated to find out how much of the blood proteins had been broken down: ordinary soap achieved little in this direction, but the proprietary cleansers did more, particularly one in which one ingredient is referred to as "enzyme".

In the second series of experiments pieces of linen were first contaminated with a virus, 4 of which were used: "ballast material" was then added, which was either blood, or a mixture of blood, faeces, albumin-lecithin and pus. After thorough drying these specimens were put through the same washing processes, and the survival or death of the virus was determined by animal or egg inoculation. Few of the results are clear-cut, most series of inoculations showing a proportion of survivors, but the authors' conclusion seems justified that 15 minutes at 80°C. will not destroy these viruses if they are heavily protected by gross soiling (*i.e.* by the repulsive quadruple mixture which formed their second "ballast material"). *L. P. Garrod*

CHAIN, E. B., PALADINO, S. & ZANCHI, F. La sterilizzazione dei terreni di cultura contenenti materiale organico solido in fermentatori da laboratorio e da impianto pilota. [**The Sterilization of Media containing Solid Organic Material in Laboratory and Pilot Plant Fermenters**] *Rendiconti Istituto Superiore di Sanità.* Rome. 1960, v. 23, Pts. 10/11, 906–14, 2 figs. (1 on folding plan). English summary.

For many fermentations culture media containing particles of such things as peanut meal or corn-meal, insoluble in water, are necessary. This is a study of the difficulties encountered in sterilizing such media and of means devised to overcome them.

Tests were carried out on a medium consisting of 3% peanut meal and 3% corn steep liquor at *p*H 6·5. This was sterilized in the various types of fermenters and when the working temperature of 30°C. had been reached, aeration and mechanical mixing were carried out. Autoclave sterilization at 120°C. was used. Peanut meal had a tendency to fall out of suspension forming a deposit, but the temperatures reached in the deposit and in the supernatant were found to be the same. There was a 12–15 minutes lag before the temperature in the fermenters reached that outside in the autoclave. Sterility tests showed that even 120°C. for 60 minutes failed to sterilize. The defect did not lie in the steel fermenters as substitution by glass containers proved to be no remedy. It appeared that in heavy deposits there would be particles enclosing spores and protecting them against moist sterilization. It was therefore decided to keep the suspension in constant agitation to break up every particle and a method to attain continuous automatic stirring was used involving pulleys and belt with an electric motor of $\frac{1}{2}$ h.p. mounted on the autoclave lid, giving 320 r.p.m. The transmission belts were not affected by repeated sterilizations. With this device, a temperature of 120°C. for 20 minutes became sufficient as was apparent if it was tested at the end of a 5-day period, although if samples were taken repeatedly through a sampling aperture over 30% of the fermenters showed contamination after 24–48 hours.

It turned out that the sampling aperture itself was the source of contamination, the valve having become crusted over with infected organic material. This difficulty was overcome by separate previous sterilization of the top part of the fermenters, including the valves in the open condition.

A similar finding depending on the same cause was found in pilot plants of 90 and of 300 ml. capacity. This was overcome by fitting to the valves steam injectors with fine nozzles from which a small, intense steam jet could be directed onto the passages preventing suspensions from settling and keeping them at sterilization temperatures. A stopcock inserted on the tubes of the steam injectors made it possible to open or shut the steam jets at any time without interrupting the main steam passage through the steam seals. The amount of steam entering the culture fluids from the nozzles of the strain injectors is so small that these can be kept open for prolonged periods during the fermentations without affecting their course. The injectors were kept going before, during and after each sample taken. *E. Agius*

CROMPTON, D. O. **Some Factors in the Prevention of Sepsis in Ophthalmic Surgery.** *Med. J. Australia.* 1961, Mar. 11, v. 1, No. 10, 356–62, 2 figs. [18 refs.]

In this paper the author correlates data previously presented by himself and others (Crompton, 1958, *Trans. Ophthal. Soc. Australia,* 1958, v. 18, 63; *ibid.,* 1959, v. 19, 48; ANDERSON, *ibid.,* 1958, v. 18, 74, JEFFS, *Australian J. Pharmacol,* 1959, new series, v. 40, old series, v. 74, 218). He lists various ways in which post-operative sepsis can occur in ophthalmic practice. In his own series of 1,411 operations from 1949 to 1960 there was no infection leading to loss of sight, whereas other surgeons in another hospital during the same period had 9 cases of post-operative panophthalmitis out of 1,321 operations. 30 out of 79 cases of panophthalmitis occurring in 344 consecutive cases of evisceration or enucleation were due to post-operative infection.

After a patient had developed a *Pseudomonas pyocyanea* infection following instillation of cocaine eye-drops this organism was recovered from the drops. On further investigation the same organism was grown from 12 out of 63 bottles of drops and *Staphylococcus aureus* from another bottle. Pseudomonads were also isolated from a stock bottle of 1% atropine closed by a bark cork, from other stock bottles and from spirit in which instruments were kept. Detailed instructions are given for the preparation of bacteriologically safe eye-drops. In most cases chlorhexidine diacetate 1 in 20,000 is used as a preservative, the drops are sterilized by conventional heat treatment methods and issued in dated bottles containing only 5 ml. Separate boiled droppers were used for each instillation.

Further investigation showed defects in aseptic techniques and sterilization procedures. Dressings drums were used in unsatisfactory autoclaves, and instruments and syringes were "sterilized" in spirit and washed in tap water. These defects were remedied along what are now conventional lines.

[There is little new in the facts reported in this paper. It is nevertheless most valuable for bringing together a body of useful information about the causes and prevention of sepsis in ophthalmic practice—in particular the detailed instructions for the preparation and use of sterile eye-drops will be found most useful.] *J. C. Kelsey*

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

VOGEL, R. A. & JOHNSON, M. **Modification of the Tellurite-Glycine Medium for use in the Identification of *Staphylococcus aureus*.** *Pub. Health Lab.* 1960, Nov., v. 18, No. 6, 131–3.

"Phenal red indicator and mannitol sugar have been added to the selective Tellurite-glycine medium for the identification of coagulase-positive staphylococci. The modified medium enables the identification of mannitol positive, coagulase positive, strains regardless of pigmentation 24 hours after the specimen is plated."

WORMALD, P. J. **Multiple Endemic Substrains of *Staphylococcus pyogenes* Phage Type 80.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1961, Mar., v. 20, 59–62.

The antibiotic patterns of strains of *Staph. aureus* phage type 80 endemic in the Salisbury area, Wiltshire, are reported. From 1956 to 1959 strains of this type had been sensitive to streptomycin. In October 1959 an outbreak of sepsis occurred in a hospital due to

strains of this type. Antibiotic sensitivities of 56 type 80 strains from this outbreak and other local sources showed 5 different apparently stable patterns. The 2 most common were distinguished by the sensitivity or resistance to streptomycin. In one lesion, strains of both patterns were found together, and their survival seemed to be evenly balanced. In this hospital outbreak, nasal colonization with the epidemic type was uncommon. *M. Patricia Jevons*

Williams, R. E. O. & Jevons, M. Patricia. Lysotypen von *Staphylococcus aureus* verschiedener Herkunft. **[Phage Types of *Staphylococcus aureus* from Different Sources]** *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 3, 349–58.

This paper from the Staphylococcus Reference Laboratory, Public Health Laboratory Service, London, gives a summary of the findings in that laboratory during the period 1954–60. Many thousands of strains examined are classified according to their source, whether from carriers or lesions, within or outside hospitals, or from epidemics of food-poisoning, and the percentage frequencies of occurrence of each individual type within 4 now recognized groups in each of these 5 categories of strains are given in a double-page table. Several distinct associations between phage type and behaviour are evident. Thus, although no less than 19 different individual types were found as causes of food-poisoning, 73·8% of the strains belonged to Group III and only 3·5 and 2·4% to Groups I and II. Group II types were much more frequently found in infections occurring outside hospitals than within them (31·3 and 11·1%): Group III, on the other hand, caused 41·4% of hospital infections and only 14·4% of those developing elsewhere. Another table states the frequency with which different individual types caused hospital epidemics: type 80 heads the list with a frequency double that of any other type, and another analysis shows that the frequency of epidemics due to this and to 52/52A/80 has increased during the period under review. Reference is made to studies showing that other types than this may be widely distributed in hospital wards, being found in the air or in the noses of numerous carriers, without causing any infections. [This paper by workers who are largely responsible for developing this method of epidemiological study gives in a few pages an impressive picture of what can be achieved by it.]
L. P. Garrod

Ritzerfeld, W. & Kienitz, M. Über die Korrelation von Enterotoxinbildungsvermögen und Penicillinresistenz bei Staphylokokken. **[The Correlation of Enterotoxin Production and Penicillin Resistance in Staphylococci]** *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 1, 29–33. [10 refs.]

This paper concerns 54 strains of staphylococci, some isolated by the authors and some obtained from collections elsewhere, including Chicago and London. According to the results of conventional biological tests for enterotoxin production and those of a test devised by themselves, depending on a characteristic respiration curve in the Warburg apparatus, they were classified into certain enterotoxin-forming strains, strains forming at the most small amounts of enterotoxin, and strains certainly forming none. The frequencies of penicillin-resistance in these 3 groups, as determined by a plate dilution test (concentrations 0·04 to 2·0 units/ml.: size of inoculum not stated) were respectively 23/26, 12/13 and 8/15. *L. P. Garrod*

Blobel, H. & Berman, D. T. **Further Studies on the *in vivo* Activity of Staphylocoagulase.** *J. Infect. Dis.* 1961, Jan.–Feb., v. 108, No. 1, 63–7, 4 figs. [12 refs.]

Rabbits were injected intravenously with 15 mgm. of alcohol-precipitated staphylococcal coagulase free from haemolytic activity [this *Bulletin*, 1961, v. 36, 73]. Estimation of total plasma protein and fibrinogen on these animals before, and at intervals after injection, showed that there was a marked decrease in plasma proteins, particularly fibrinogen. This was maximal at 2 hours and normal values were regained after 3 days. No such drop was demonstrated, on challenge, in an animal hyperimmunized with purified coagulase and levels remained normal on injection of a control rabbit with the supernatant of a broth culture of a coagulase negative staphylococcus.

Death occurred in 90 minutes on injection of lethal doses of coagulase (20–50 mgm.). There was almost complete fibrinogen depletion and considerable decrease in total protein. At autopsy 1 or more lobes of the lung were seen to be oedematous and there were homogeneous intravascular coagula. These were shown to contain coagulase by the use of fluorescein-labelled anticoagulase.

[See also Smith and Johnstone, this *Bulletin*, 1958, v. 33, 794. For earlier studies, see this *Bulletin*, 1961, v. 36, 287.] *M. Patricia Jevons*

Fisher, S. **A Heat Stable Protective Staphylococcal Antigen.** *Australian J. Exper. Biol. & Med. Sci.* 1960, Dec., v. 38, Pt. 6, 479–85.

A coagulase positive strain of *Staphylococcus aureus*, the mouse virulence of which was markedly enhanced by mucin, was grown in sloppy agar. Supernatant fluids were shown to be of low toxicity, and were used to immunize mice by single subcutaneous injections of 0·5 ml. amounts of various dilutions from 1/10 to 1/25,000. Animals were challenged intraperitoneally 10 days later with 100 LD50 of the homologous organism suspended in mucin. Protection was complete in animals immunized with 1/10 and 1/100 dilutions and partially with 1/5,000 dilution. Immunity developed in about 4 days and lasted for at least 6 weeks.

Serum from immunized mice passively protected normal mice, and passive protection tests showed that immunity could also be produced in a goat although this took longer to develop. The immunizing antigen

was shown to be resistant to 10 minutes in a boiling water bath and to be non-dialysable.

[For an earlier study see also this *Bulletin*, 1961, v. 36, 288.] *M. Patricia Jevons*

SMITH, I. M., WILSON, Ann P., HAZARD, E. C., HUMMER, W. K. & DEWEY, Mary E. **Death from Staphylococci in Mice.** *J. Infect. Dis.* 1960, Nov.–Dec., v. 107, No. 3, 369–78, 3 figs. [12 refs.]

Mice were injected by various routes with cultures containing about 10^8 staphylococci. Injection into the peritoneal cavity, heart, spleen, liver or brain was commonly followed by the death of a large proportion of the animals within 24 hours. The death rate after intravenous or intranasal injection was much lower, and death was delayed for several days. Intramuscular, subcutaneous and oral inoculation killed no mice, but when the dose was increased to 10^{10}–10^{12} even these routes proved fatal.

Earlier experiments [SMITH and DUBOS, this *Bulletin*, 1956, v. 31, 673] illustrating differences in the fate of staphylococci in different organs were confirmed, but no organ showed a high multiplication rate after introduction of the cocci by all the different routes tested.

The total body content of staphylococci, determined by grinding the carcass in a Waring blendor, increased to reach about 10^9–10^{10} organisms at the time of death. Mice could not, however, be killed in less than 60 minutes even by the injection of 10^{11} cells.

R. E. O. Williams

CASSINGENA, R., ORTALI, A. V., VILLA, L. & MILAZZO, M. ***Micrococcus violagabriellae* (Castellani, 1955).** *Rendiconti Istituto Superiore di Sanità.* Rome. 1960, v. 23, Pts. 10/11, 964–77, 2 figs. [22 refs.] English summary.

This is a study of a micro-organism resembling *Staphylococcus*, isolated by CASTELLANI, in 1955, from erythema in the axilla and, in 1957, from cases of scalp furunculosis. The 6 original Castellani strains were used (*Ann. Inst. Pasteur*, 1955, v. 89, 475; *Bact. Proc.*, 1957, p. 98).

They were found to have a staphylococcal morphology, but colonies were smaller (0·1–0·2 mm.) They grew well on Chapman's medium with 8% of salt, with an optimum at 1 to 2%. Unlike the staphylococcus, *Micrococcus violagabriellae* could not use mannitol. Action on 23 sugars is given in a table, which shows identical behaviour by all 6 strains. They are indole and coagulase negative, reduce nitrates, are phosphates, urease, and oxidase negative, non-haemolytic, produce fibrinolysin and H_2S, do not attack gelatin and coagulate milk. Their characteristic ability to produce a violet-red pigment is brought out by culture on agar containing an iron salt, such as iron-ammonium citrate at 0·05%. Colour is also produced on potato.

Micrococcus violagabriellae appears to share some antigens with *Staphylococcus* but has others peculiar to itself. It did not appear to be pathogenic to rabbits. The authors did not repeat Castellani's experiment proving the micro-organism's pathogenicity for human beings. The micro-organism is sensitive to chloramphenicol, dihydrostreptomycin, erythromycin, and penicillin. It is susceptible to an adapted phage derived from the Vuitton anti-staphylococcal phage supplied by the Paris Institut Pasteur.

The authors support Castellani's view considering *Micrococcus violagabriellae* a definite species.

E. Agius

ZAMPIERI, A., VELLA, L. & MERUCCI, P. Coltura dello streptococco emolitico di gruppo A in terreno chimicamente definito a base di purine e pirimidine. **[Cultivation of Haemolytic Streptococci of Group A on a Chemically Defined Purine and Pyrimidine Medium]** *Rendiconti Istituti Superiore di Sanità.* Rome. 1960, v. 23, Pts. 10/11, 983–92, 2 figs. [21 refs.]

An attempt to study the production by haemolytic streptococci especially of lytic toxic agents such as streptolysin O and S showed that no chemically defined synthetic medium had yet been described.

The work was carried out with 5 standard strains of Group A *Streptococcus pyogenes*, whose virulence after at least 10 subcultures was tested on mice. After various trials, a medium referred to as SPP, made up as follows, was found to grow *Streptococcus* without altering its characteristics:

Solution A: NaCl 6 gm.; KCl 0·4 gm.; KH_2PO_4 0·6 gm.; $Na_2HPO_4.2H_2O$ 0·6 gm.; cystine 0·05 gm.; distilled water 200 ml.; sterilized at 115°C.

Solution B: Uracil 25 mgm.; cytosine 12 mgm.; thymine 3 mgm.; adenine 1·5 mgm.; guanine 1 mgm.; $MgSO_4.7H_2O$ 0·25 gm.; distilled water 200 ml.; sterilized at 115°C.

Solution C: Choline 0·07 mgm.; folic acid 0·1 mgm.; nicotinamide 0·25 mgm.; pantothenate 0·25 mgm.; riboflavine (amount not given through a printing error); pyridoxine 0·1 mgm.; thiamine 0·5 mgm.; L-glutamine 25 mgm.; distilled water 100 ml.; sterilized by Seitz filtration.

Solution D: $NaHCO_3$ 0·5 gm.; hydroximethylaminoethane 1·21 gm.; distilled water 200 ml.; sterilized by Seitz filtration.

Solution E: Glucose 15 gm.; starch 10 gm.; $CaCl_2$ 0·18 gm.; vitamin B_{12} 0·5 mgm.; distilled water 300 ml.; sterilized at 115°C.

The solutions are mixed with sterile precautions, *p*H is adjusted to 7·2 by N HCl, the volume brought up to a litre and distributed in 100 ml. lots in flasks. In practice it was found convenient to prepare the vitamin solution a 1,000 times more concentrated and to keep it at −30°C. The purine and salt solutions were made a 100 times more concentrated. The L-glutamine solution was prepared separately.

Close control showed that this purine and pyrimidine medium grows β-haemolytic Group A streptococci almost as well as TODD and HEWITT'S classic heart infusion medium. The fact that the growth curve with the synthetic medium does not rise as high as that with the biological medium appears attributable to a too rapid lowering of *p*H. Addition of minimal traces of

$FeSo_4.7H_2O$ and $MgCl_2.4\ H_2O$ (0·005 gm. per litre) produced a wider zone of haemolysis on blood agar. Use of the synthetic medium also showed that the usually exacting streptococcus could grow in the absence of aminoacids except for glutamine and cystine, which latter acts mostly as a reducing substance.

It is on the purine (adenine and guanine) and pyrimidine (cytosine, thymine, and uracil) basis that the nitrogen metabolism of the strain depends. An excess, even in one of them will stop growth in the first phases of multiplication. A deficiency reduces the yield. Uracil and cytosine were shown to be essential factors whereas adenine and thymine can be considered stimulating factors.

In this medium the streptococcus is capable of synthesizing aminoacids by metabolic routes involving the purine NH_2 group. L-glutamine was indispensable, although its concentration could be reduced to one-tenth if growth was in 5% CO_2. Vitamins in the medium are indispensable to growth even though they may not all be used up in the process. While no growth will result in the absence of pantothenate, nicotinamide, folic acid and pyridoxine, it will only be reduced in the absence of choline, riboflavine, thiamine and vitamin B_{12}. Glucose in a concentration of 1·5% is the source of energy for the synthesis of the micro-organism, which converts 95% of it to lactic acid. Starch was added because it gives a better yield probably through an effect of " collodial " protection. Mucin could be an alternative but was not used as it was not available in sufficiently pure form. *E. Agius*

Lian, T. S. & Pierce, W. A., Jr. **A Study of Bentonite Flocculation Test for Measurement of Type-Specific Streptococcal Antibodies.** *Proc. Soc. Exper. Biol. & Med.* 1961, Jan., v. 106, No. 1, 207–11. [18 refs.]

The demonstration of type specific antibodies to Group A streptococci in human sera is difficult and time consuming. The authors explore the possibility of using the bentonite flocculation test [*Trop. Dis. Bull.*, 1952, v. 49, 431] for this purpose.

The M antigens of 3 strains of streptococci (Types 12, 14 and 36) were extracted by hot acid and partially purified by repeated alcohol precipitation until free from group polysaccharide. Stock bentonite suspensions were sensitized with these antigens by mixing and leaving in the refrigerator overnight. After the addition of methylene blue the mixture was shaken, centrifuged and the deposit washed in saline. The sensitized particles were resuspended in phosphate buffer at *p*H 8·5 and normal rabbit serum. This test antigen could be stored for 6 weeks.

A drop of test antigen was mixed with a drop of various dilutions of unadsorbed rabbit anti-M serum prepared against the 3 test strains. Tests were carried out on a slide which was rotated for 15 minutes and examined for flocculation microscopically.

Titres were low compared with titres obtained with an antigen of sensitized tanned red cells (Denny and Thomas, *J. Clin. Invest.*, 1953, v. 32, 1085) [Holmes, this *Bulletin*, 1959, v. 34, 492] the highest titre with homologous antiserum was usually 1 in 32 and there were cross reactions. These were non-reciprocal between T36 and T14 antigens. No flocculation occurred when bentonite was sensitized with crude acid extracts containing both M and Group A polysaccharide tested with type-specific antisera or when sensitization was with group polysaccharide tested with group-specific antiserum.

[No human sera were tested but even with specially prepared streptococcal rabbit antisera titres were low and there was a lack of specificity.]

[See also this *Bulletin*, 1959, v. 34, 1288.]

M. Patricia Jevons

Vella, L., Zampieri, A. & Merucci, P. Inibizione dell'azione emolitica della O-streptolisina mediante cardiolipina. **[Inhibition of the Haemolytic Action of O-Streptolysin by Cardiolipin]** *Rendiconti Istituto Superiore di Sanità.* Rome. 1960, v. 23, Pts. 10/11, 978–82. [12 refs.] English summary (3 lines).

0·5 ml. volumes of O-streptolysin containing 1 haemolytic unit (2 reconstituted lyophilized toxins obtained from reliable commercial firms being used) were tested by being placed in contact with volumes of cardiolipin ranging from 0·1 to 0·8 ml. at a 1/10 and at a 1/20 dilution. The mixtures were brought up to 1·5 ml. volumes by buffer solutions and incubated, after shaking, at 37°C. for 15 minutes. 0·5 ml. volumes of 4% washed rabbit cells were then added. The mixture was incubated for 45 minutes, then placed at 4°C. for 4 hours and read, the cells being counted in a Burker chamber. A marked inhibitory power of the haemolytic action of O-streptolysin, increasing with the concentration of cardiolipin up to a maximum of inhibition allowing survival of 46% of red cells was noticed.

The value of this investigation would lie in its attribution to cardiolipin set free from the perfused heart of the inhibitory action on the haemolytic action of O-streptolysin in perfusion experiments. *E. Agius*

Tacquet, A. & Tison, F. Résultats de l'isolement du bacille tuberculeux dans 55,000 crachats par le Teepol 410 basique. Influence du milieu de culture. **[Isolation of Tubercle Bacilli in 55,000 Sputum Specimens by means of Basic 410 Teepol. Influence of the Culture Medium]** *Ann. Inst. Pasteur.* 1961, Feb., v. 100, No. 2, 153–8. [11 refs.]

The Teepol method originally published in 1954 [Tison, this *Bulletin*, 1955, v. 30, 1106] has now been used for culturing 55,000 specimens of sputum, and from these experiences the authors maintain that although it is one of the mildest of methods for treating specimens of sputum, the contamination rate is very low; of the first 1,000 specimens treated in 1960, only 6 were contaminated. The increase in positive results under practical conditions is approximately 20% over the more usual methods of treatment.

Teepol is not a standard product and as its composition varies, it is important that the type with the correct

composition be used; in France this is Teepol T 410. With small inocula it is also important to use an egg medium, *e.g.* Löwenstein medium, because traces of Teepol carried over in the inoculum may inhibit growth especially in such media as that of Dubos, with or without agar; on egg media the inhibiting effect is less. The inhibition is apparently due to the lauryl sulphate ion rather than to the surface-activity of the Teepol.

S. R. M. Bushby

Rei, T. S. **The Effect of Rotation Aeration on the Growth of *Mycobacterium tuberculosis*.** *Japanese J. Microbiol.* 1959, Oct., v. 3, No. 4, 509–32, 5 charts & 12 graphs. [32 refs.]

This lengthy paper describes 6 experiments in which 8 strains of tubercel bacilli were grown in 7H-9 Tween-albumin medium, rotating at 16–18 r.p.m. Stationary cultures served as controls, and the extent of growth was determined turbidometrically in a spectrophotometer.

With stationary cultures, by noting the time that the growth from minimal inocula took to become visible, the 7H-9 medium was shown to be superior to oleic acid-albumin or Sauton media; the respective generation times were calculated as 13, 14·4 and 21–25 days. Rotating the cultures decreased the generation time, lengthened the period of logarithmic phase of growth and increased the yield of bacilli, and adding glucose and glycerol to the medium, even in concentrations that were inhibitory in stationary cultures (0·5%), increased further the growth. The enhancement by rotation was greatest with the more slowly growing strains such as the Ravenel bovine strain. The growth in the stationary cultures was increased by sloping the tubes but it was still inferior to forced aeration by rotation, and in a final experiment, growth that had ceased in stationary cultures was shown to re-commence and proceed at a rapid rate when the tubes were rotated.

S. R. M. Bushby

Paas, Cornelia M. S., Flick, J. A., Kapral, F. A. & Rudd, Joanne H. **On the Persistence of Tuberculin in Hypersensitivity in Guinea Pigs made Sensitive Passively.** *Amer. Rev. Respiratory Dis.* 1961, Mar., v. 83, No. 3, 372–80. [21 refs.]

"Normal guinea pigs were passively sensitized to tuberculin by transfer of peritoneal exudate and splenic cells from actively sensitized donors. At intervals, paracentesis was performed on the recipients, and the mononuclear cells were examined for sensitivity to PPD in tissue culture. Skin tests were performed at various times.

"Prolonged sensitivity can be demonstrated without bringing the recipient into contact with the antigen by skin testing. The possibility of active sensitization by antigen transfer to the recipient via donor cells appears to be unlikely, but cannot be excluded entirely. Hypersensitivity seems to be transferred to the recipient's mononuclear cells, so that they themselves become reactive to PPD in tissue culture. The duration of passively transferred hypersensitivity may exceed several months."

Kunz, H. H. & Rudnick, Hildegard. Untersuchungen über den Vertikaldiffusionstest zur Resistenzprüfung von Tuberkelbakterien. **[Investigations of the Vertical Diffusion Test for the Determination of the Resistance of Tubercle Bacteria]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 4, 522–9, 5 figs.

A special tube is used for this test with an internal projection which enables a liquid egg medium to be "sloped" in a horizontal position before autoclaving. The water of condensation is then removed and replaced with 0·5 ml. of a solution containing streptomycin, PAS, isoniazid or Conteben, the concentrations of these in μgm./ml. being respectively 1,000, 100, 20 and 170. The medium is then inoculated with the strain of tubercule bacillus to be tested, care being taken not to contaminate the upper part of it with the drug solution. This diffuses upwards through the medium, and the height of the area in which growth is inhibited is a measure of sensitivity. A diagram is given showing the levels indicating different degrees of resistance for each drug: it appears from this that PAS and isoniazid diffuse further than the others. Most of the paper is devoted to results of parallel tests of numerous recently isolated strains conducted both by this and a conventional tube dilution method, in either the same or different laboratories. Concordance was good, and the authors maintain that the vertical diffusion test is as reliable as a dilution test, as well as being easier to perform.

L. P. Garrod

Botez, Virginia, Angelesco, I., Bonciu, C., Paraschivesco, Maria, Nafta, I. & Petrovici, Monica. Méthodes d'étude du vaccin BCG. II-e Mémoire. Tests expérimentaux sur cobayes (réaction locale, allergie et test de protection). **[Methods of Studying BCG Vaccine. Second Report. Experimental Tests in Guineapigs (Local Reaction, Allergy, and Protection Test]** *Arch. Roumaines Path. Expér et Microbiol.* 1960, Dec., v. 19, No. 4, 551–61.

This paper reports the results of examining 7 batches of freeze-dried BCG vaccine, kept for 0–18 months at 4°C., and 7 batches of fresh vaccine, kept under similar conditions for 1–14 days; the suspending agent for the dried vaccine was 10% saccharose and 1% gelatin. In all, 600 guineapigs were vaccinated and 50–79 days later challenged with 0·01–0·001 mgm. of virulent tubercle bacilli, injected subcutaneously; tuberculin tests, with 1 in 10 titration were done 30 days after vaccination. The effectiveness of the vaccines was assessed by the duration of the BCG lesion, the degree of hypersensitivity, the extent of protection afforded against challenge, judged by survival time and the extent of the tuberculous lesions, and the persistence of the local ulcer following the reinfection with the virulent strain.

The authors conclude that although no single test

is sufficient for evaluating the vaccine, the protective test is the most valuable, but histological examination of the tissues is essential; results show that the 2 forms of the vaccine examined were equally effective.

S. R. M. Bushby

EUSTATZIOU, Silvia, MEITERT, Eugenia, TULPAN, Gertruda, ANTOHI, Maria & EUSTATZIOU, G. Contribution à l'étude des souches de *Mycobactéries saprophytes* et *atypiques*. Note I. Étude des caractères morphologiques, culturels, biochimiques et de la sensibilité aux antibiotiques. [**Study of Saprophytic and Atypical *Mycobacteria*. I. Morphological, Cultural, and Biochemical Characters and Sensitivity to Antibiotics**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Dec., v. 19, No. 4, 583–600. [18 refs.]

These examinations were made on 39 strains of named saprophytes, originally obtained from various European institutes, and 13 atypical mycrobacteria from pathological specimens from patients at the Institut de Phtisiologie, Bucharest. Based on the classification of GORDON and SMITH (*J. Bacteriology*, 1953, v. 66, 41 and 1955, v. 69, 502), 5 of the saprophytes were classed as *Mycobacterium phlei*, 25 as *Myco. smegmatis*, 1 as *Myco. fortuitum;* 6 strains did not conform to this classification and were placed in the species *Myco. pellegrini*, and 2 did not fit into the classification scheme.

None of the saprophytes or the atypical mycobacteria decomposed casein or gelatin and only the strains of *Myco. pellegrini* and one strain of *Myco. smegmatis* hydrolysed tyrosine. 5 of the *Myco. smegmatis* strains, 1 of the *Myco. pellegrini* and 1 of the atypical strains hydrolysed amidone. All the strains of *Myco. phlei, Myco. pellegrini* and *Myco. smegmatis* grew at 14°C.–45°C. and some of them grew at 52°C. The 1 strain of *Myco. minetti* examined grew only between 14°C. and 40°C. and the 1 strain of *Myco. battaglini* grew only at 37°C. and 45°C. The strain of *Myco. thamnopheos* grew at 14°C. and 37°C. The atypical mycobacteria showed variable growth temperature ranges, varying from 14°–45°. Only 1 strain withstood heating at 60°C. for 4 hours and this was a strain of *Myco. phlei*.

The atypical mycobacteria showed little ability to ferment the 14 sugars used; 1 fermented glucose, maltose, mannose, raffinose and trehalose, another fermented glucose and trehalose, a third fermented sorbitol and xylose, and a fourth fermented only glucose. The saprophytes were much more strongly saccharolytic, but none fermented lactose. Of the saprophytes, all were also able to utilize citrates and succinates and only the strains of *Myco. phlei* were unable to use benzoates; the atypical mycobacteria were unable to utilize any of these organic acid anions. All the strains were catalase positive, and all except one of the atypical mycobacteria reduced nitrates.

The sensitivity of the atypical mycobacteria to PAS, streptomycin, isoniazid, oxytetracycline, chloramphenicol and TB1 was so variable that sensitivity tests were of little value in classifying these organisms.

S. R. M. Bushby

GÜRSEL, A. Les caractères bacteriologiques, cytologiques, biochimiques et la pathogenicité pour les animaux de laboratoires des souches A.A.R. dites atypiques isolées en Turquie. [**The Bacteriological, Cytological, Biochemical Features and Pathogenicity for Laboratory Animals of Atypical Acid Fast Bacteria isolated in Turkey**] *Türk Ijiyen ve Tecrübî Biyoloji Dergisi*. Ankara. 1960, v. 20, No. 3, 386–404. [75 refs.] [Fuller version in Turkish 367–85.]

This report comes from the Central Institute of Hygiene, Ankara, and is concerned with the atypical acid-fast bacilli isolated since 1957; the incidence of these strains was 4 of 546 acid-fast bacilli isolated in 1957, 14 of 652 strains in 1958, 15 of 748 in 1959; of these 33 strains, 32 have been studied.

16 of the strains were photochromogens (Group I), 11 were scotochromogens (Group II), 4 were non-pigmented (Group III) and 1 was a rapid-grower (Group IV). The morphology of the strains was variable, but only the photochromogens showed cording, 8 fairly strongly and 4 weakly. None of the strains was strongly neutral red positive, but 7 of the scotochromogens were weakly positive; all the strains were strongly catalase positive. All the strains were resistant to 25 μgm. isoniazid per ml., 10 μgm. streptomycin per ml. and 10 μgm. PAS per ml. None of the strains produced progressive disease in guineapigs, the only lesions usually being an enlargement of the lymphatic glands; in mice, some of the photochromogens produced renal abscesses.

22 of the strains were from men, and 24 were from patients aged 26–45.

S. R. M. Bushby

DAOD NATHOO, F., DODIN, A. & BRYGOO, E. R. Recherches sur les antigènes de *Pasteurella pestis*. II. Étude par précipitation en gélose de deux sérums antipesteux avant et après saturation par des extraits A.R.N. et A.D.N. [**Studies on the Antigens of *Pasteurella pestis*. II. Gel Precipitation of Two Anti-Plague Sera before and after Saturation with RNA and DNA Extracts**] *Arch. Inst. Pasteur de Madagascar*. 1960, v. 28, 11–13.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 908.]

DODIN, A. & BRYGOO, E. R. Étude quantitative de l'utilisation des sucres par *Pasteurella pestis* souche E.V. en suspension non proliférante. III. Le xylose. IV. Le mannose. V. La glucosamine. [**Quantitative Study of Glucide Uptake by *Pasteurella pestis* EV Strain in Non-Proliferating Suspensions. III. Xylose. IV. Mannose. V. Glucosamine**] *Inst. Pasteur de Madagascar*. 1960, v. 28, 15–16.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 908.]

Souza Santos, P., Vallejo-Freire, A., Furlanetto, R. S. & Andrade, M. C. **Studies on the Adsorption of Diphtheria Toxoid by Aluminum Oxide Hydrate Gels.** *Mem. Inst. Butantan.* 1959, v. 29, 197–212. [25 refs.]

"1. Phosphate ion has a strong inhibiting power on the adsorption of diphtheria toxoid by aluminium hydroxide gels of different crystalline structures and surface areas.

"2. The probable mechanism of inhibition is the blocking of aluminum ions from the A100H or $Al(OH)_3$ molecules on the surface of the colloidal particles due to the formation of an insoluble aluminum phosphate, probably variscite—$Al(OH)_2 \cdot H_2PO_4$.

"3. Chloride, glycine, acetate and sulphate ions do not have a noticeable inhibiting effect on the adsorption of toxoid by aluminum hydroxide gels; ferrocyanide ion has a small inhibiting power, but in smaller degree than phosphate ion. In media containing these ions, the adsorption of toxoid follows roughly a chemisorption isotherm with a maximum value for the adsorptive power. This adsorptive power of the different aluminum hydroxides is directly proportional to the surface area of the gel or inversely proportional to the average particle size; no direct relation was found between the crystalline structure and adsorptive power of the different aluminum hydroxide gels.

"4. Adsorptive powers for toxoid ranging between 800 and 1,000 Lf units per milligram of Al_2O_3 were found with amorphous aluminium hydroxide precipitated 'in situ' from diphtheria toxoid dissolved in glycine-acetate buffer of pH 7·1, using aluminum chloride and ammonium hydroxide solutions as precipitants; potassium hydroxide solutions give amorphous aluminum hydroxide gels with smaller adsorptive power than precipitates from ammonium hydroxide solutions; this adsorption can be completely inhibited by phosphate ions; aluminum complexing ions such as tartrate, citrate and oxalate prevent precipitation of aluminum hydroxide and no toxoid is adsorbed."

Munoz, J. & Maung, M. **Anaphylaxis in *Bordetella pertussis*-treated Mice. IV. Schultz-Dale Reaction.** *Proc. Soc. Exper. Biol. & Med.* 1961, Jan., v. 106, No. 1, 70–73. [10 refs.]

The injection of *Bordetella pertussis* cells into mice enhances antibody response to various antigens [this *Bulletin,* 1958, v. 33, 885] and most likely increases the susceptibility of mice to active anaphylaxis by stimulating antibody response to sensitizing antigen. This set of experiments was designed to study the effect of *B. pertussis* cells on specific active and passive sensitization of smooth muscle as demonstrated by the Schultz-Dale reaction. One result was to show the importance of using homologous antibody in studying anaphylactic reactions in mice: mouse antibody was found to be more effective than rabbit antibody in sensitizing the mouse uterus to specific antigen. *B. pertussis* cells did not affect the sensitization of the mouse uterus when the mouse was sensitized by passive means, but they accelerated the appearance of sensitivity of the muscle when the active method of sensitization was employed, an observation that can be explained by the known adjuvant action of *B. pertussis* cells. *D. A. Cannon*

Kleinmaier, H. & Schubert, R. H. W. Zur Differentialdiagnose von *Pseudomonas aeruginosa* [**Differential Diagnosis of *Ps. aeruginosa***] *Arch. f. Hyg. u. Bakt.* 1961, Mar., v. 145, No. 2, 108–36, 9 figs. [29 refs.]

The authors discuss at great length the differential value of (a) the cytochrome oxydase test: (b) the lecithinase test in egg-yolk media, and (c) the production of diketo gluconate and slime formation in media containing 0·05% K gluconate. These have been described in the literature as differential tests for distinction between *Ps. pyocyanea* and other pseudomonads.

Their general conclusions are: (i) that *Ps. putida* is differentiated from *Ps. fluorescens* and *Ps. pyocyanea* by the lecithinase and slime formation tests; (ii) that a limited differentiation between *fluorescens* and *pyocyanea* is observed with these tests but since it is largely conditioned by temperature the capacity of growth at 41°C. is the more valuable differential feature of *Ps. pyocyanea.*

These observations applied equally to strains of *Ps. pyocyanea* which failed to produce pyocyanin. The cytochrome oxydase test was positive with all 3 forms of pseudomonads. The value of tetramethyl-p-phenylenediamine hydrochloride as a reagent in this test appears to have been overlooked. *J. W. McLeod*

Kranendonk, O. & Van Noord, H. **Transport in the Tropics of Faecal Samples for Bacteriological Examination for Typhoid and Paratyphoid Fever and Bacillary Dysentery.** *Trop. & Geograph. Med.* Amsterdam. 1960, Dec., v. 12, No. 4, 345–55. [13 refs.]

This article reports the comparative trials of 5 different transport media on faecal specimens from persons known to be excreting either salmonellae or shigellae as a result of a natural infection or a carrier condition. The 5 media used were: Selenite-pre-cultivation medium, Stuart transport medium [Stuart *et al.*, this *Bulletin,* 1954, v. 29, 730], Teague and Clurman buffered glycerol-saline medium, silica-gel dry medium and the dry faecal specimen on filter paper [*ibid.,* 1950, v. 25, 1064]. All specimens were stored at 30°C. during the day and at 20°C. at night. Relative humidity varied from 40–50% during the day to 50–70% at night and the samples were kept under these conditions for 1, 2 and 4 weeks.

The overall results with the salmonella organisms, including the typhoid-paratyphoid group, were better than with the shigellae and the selenite-pre-cultivation medium gave better results than any of the other transport media. Even after 4 weeks storage positive

isolations were fairly regularly obtained. The results with the dysentery bacilli, all of which were *Shigella sonnei*, were far less satisfactory but here again the selenite medium was superior, with Stuart's medium in second place. The influence of humidity on the filter-paper technique was particularly marked.

So long as the specimen was placed in the transport medium as soon as possible after being passed the delay in transportation did not seem so important with salmonella infections, but with the shigella strains tested speedy dispatch was most important. The best results were obtained with specimens stored in a combination of transport-media. *H. J. Bensted*

SEELIGER, H. P. R. & HOLL, K. M. Zur Differentialdiagnose von Enterobacteriaceen mit dem Lysin-Decarboxylase-Test. [**Differential Diagnosis of Enterobacteriaceae by the Lysin Decarboxylase Test**] *Ztschr. f. Hyg. u. Infektionskr.* 1961, v. 147, No. 4, 336–46. [20 refs.]

In differentiating some salmonella-like strains, notably paracolon strains of the Citrobacter group, the Bethesda-Ballerup and the Freundii groups of coliforms; the test of Carlquist has been found useful. This is the LDC or lysin decarboxylase test.

The details of media and methods of detecting the decarboxylation of lysin with amine formation used by various workers are described. In the simplest of these, Falkow's, a Bacto peptone and yeast extract medium containing 0·1% of glucose and 1·0% of lysin and brom-cresol-purple as indicator—is first acidified and then turned alkaline by bacteria provided with the decarboxylase in question, with other bacteria it remains acid.

Both Falkow's and Carlquist's methods showed all Citrobacter strains as negative but Carlquist's was most reliable in the regularity with which Salmonella strains were positive (99%). A group of Arizona and one of Hafnia strains also gave positive results.

The test is recommended as a useful one in eliminating strains of the Citrobacter group suspected to be salmonellae. *J. W. McLeod*

NIKAIDO, H.; FUKASAWA, T. **Galactose-Sensitive Mutants of *Salmonella*. I. Metabolism of Galactose** [NIKAIDO]. *Biochim. et Biophys. Acta.* 1961, Apr. 15, v. 48, No. 3, 460–69, 1 fig. [38 refs.] **II. Bacteriolysis induced by Galactose** [FUKASAWA & NIKAIDO]. *Ibid.*, 470–83, 7 figs. [40 refs.]

MAGWOOD, S. E. & ANNAU, E. **The Adsorption of Somatic Antigens of *Salmonella* by Polystyrene Latex Particles.** *Canadian J. Comp. Med.* 1961, Mar., v. 25, No. 3, 69–73, 4 figs. [10 refs.]

"A latex agglutination test for the detection of Salmonella antibodies in turkey antisera is described. Crude and partially purified extracts containing Salmonella somatic antigens were found to be adsorbed by polystyrene latex particles (diameter 0·557 and 1·171 microns). The particles so treated acquired a serologic specificity and were agglutinated by antibodies for the homologous Salmonella groups.

"Latex suspensions sensitized with one to three bacterial extracts gave serum agglutination titers equal to those observed with the corresponding individual bacterial antigens."

KOTELKO, K., STAUB, A. M. & TINELLI, R. Étude immunochimique sur les *Salmonella*. VIII. Role des groupements O acétyls dans la spécificité du facteur O: 5. [**Immuno-Chemical Studies on *Salmonella*. VIII. Role of O Acetyl Groupings on the Specificity of Factor O: 5**] *Ann. Inst. Pasteur.* 1961, May, v. 100, No. 5, 618–37, 4 figs. & 3 pls. [23 refs.]

DIGEON, Monique & RAYNAUD, M., with the technical collaboration of Jeanne RIZA. Toxicité et virulence comparées des formes smooth et rough de *Salmonella typhi* sur embryon de poulet. [**Comparative Toxicity and Virulence of Smooth and Rough Forms of *Salmonella typhi* in Chick Embryos**] *Ann. Inst. Pasteur.* 1961, Mar., v. 100, No. 3, 344–51. [11 refs.]

Using 10-day embryonated hens' eggs the authors found that the chick embryo was equally sensitive to the endotoxin extracted from smooth strains of *Salmonella typhi* and that extracted from rough strains of this organism when these preparations were injected intravenously in equivalent dosage; expressed as the LD50 the dose was of the order of 0·01 μgm. When, however, chick embryos were injected intravenously with living cultures of the rough strain (R2), the smooth Vi-negative strain (O 901) and the Vi-positive strain (Ty 2) the embryos withstood higher doses of R2 than either O 901 or Ty 2. With an estimated dose of living organisms of 2–10 bacteria injected intravenously the mortality of the embryos was: with Ty 2 8 of 10 died, with O 901 12 of 12, with R2 4 of 20 died.

The results of injections into the yolk sac were of considerable interest. The yolk sac did not appear to be very sensitive to different doses of endotoxin unless the differences were great, but it was, on the other hand, very sensitive to quite small doses of living bacteria. Injection into the yolk sac of about 4 viable bacteria of either rough or smooth cultures killed approximately 100% of the embryos in 18–24 hours with very great multiplication of the organisms—the amniotic fluid containing more than 100×10^6 organisms per ml. It is not reported whether there was any evidence of R−S change. Curiously enough experiments with chorioallantoic injections were less satisfactory. While the CAM was very sensitive to Vi-positive strains, it appeared to be less sensitive to smooth Vi-negative cultures and the sensitivity to rough cultures was most irregular, extremely large doses sometimes failed to kill the embryos. FINKELSTEIN and RANSOM have used the chick embryo for experiments with *Vibrio cholerae* and *Escherichia coli*

[*Trop. Dis. Bull.*, 1961, v. 58, 196] and the method may well have other interesting applications.

H. J. Bensted

MITSUHASHI, S., HASHIMOTO, H. & KAWAKAMI, M. **Experimental Typhoid. Anti-Lethal Resistance of Mice immunized with Live Vaccine against Infection with *Salmonella enteritidis*.** *Japanese J. Exper. Med.* 1960, Oct., v. 30, No. 5, 375–84, 5 figs. [38 refs.]

There have been several papers dealing with experimental infections of mice with *Salmonella enteritidis* and associated problems by this group of workers during the last few years [see this *Bulletin*, 1959, v. 34, 926; 1960, v. 55, 394]. The present paper is mainly concerned with the high degree of resistance to further infection that develops in mice immunized with living vaccines. Immunization of mice with killed *Salm. enteritidis* vaccines does not induce a high degree of resistance against a virulent challenge, but immunization with a living vaccine gives to mice the power to resist infection with an intravenous challenge with a dose of 1,000 MLD of a virulent strain without loss of body weight. Mice surviving the intravenous injection of 1,000 MLD of the virulent strain were found to resist a virulent intravenous challenge of 10,000 MLD. It should be noted that the hyper-immunization schedule of the mice commenced with intraperitoneal injections of living cultures of an attenuated strain. Mice immunized with endotoxin preparations of *Salm. enteritidis* will develop resistance against the lethal effects of the endotoxin but not against infection with the virulent challenge. *H. J. Bensted*

BREDE, H. D. *Salmonella Stellenbosch*—'n nuwe serotipe. **[Salmonella Stellenbosch, a New Serotype]** *South African Med. J.* 1961, Apr. 1, v. 35, No. 13, 267–8, 1 fig.

The English summary appended to the paper is as follows:—

"A new serotype, *Salmonella stellenbosch* (1, 9, 12 : z : 1, 7) was isolated from the faeces of a coloured man who for 2 months, had suffered from severe diarrhoeas. The patient came from the environment of Stellenbosch.

"The culture possessed biochemical characteristics typical of the salmonella group.

"On serological examination *Salmonella stellenbosch* was strongly agglutinated by the O-antisera 1, 9 and 12. Examination of the H antigen showed that the organism was diphasic. Phase 1 was agglutinated by z-antiserum. Phase 2 was agglutinated by the unspecific antisera 1 and 7. Phase 2 (1, 7) of *Salmonella stellenbosch* is identical with phase 2 (1, 7) of *Salmonella kaapstad*.

"The antibiogram of *Salmonella stellenbosch* is typical for a salmonella. The strain is resistant to penicillin, erythromycin, ilotycin, kanamycin and albamycin, but sensitive to streptomycin, chloramphenicol, and the tetracyclines."

STENZEL, W. Über die pathogenetische Bedeutung des thermolabilen Eiweisstoxins der *Sh. dysenteriae* 1. **[The Pathogenic Significance of Thermolabile Protein Toxin from *Shigella dysenteriae* 1]** *Ztschr. f. Hyg. u. Infektionskr.* 1961, v. 147, No. 3, 240–45. [27 refs.]

Two strains of Shiga dysentery bacilli were used for toxin production; one proved capable of invading mucous membranes in animal experimental work, the other was devoid of this capacity. The conjunctiva and the bladder were the mucous membranes tested. Surprisingly the most active toxin was obtained from the apparently less pathogenic strain. Toxin protein was prepared by a series of trichloracetic acid precipitations followed by extraction of the precipitates with dilute solutions of $NaHCO_3$, and a final precipitation with acetone, all operations being carried out at low temperatures. The most effective products had a LD50 dose of 1 μgm. for the mouse.

It was not found, however, after immunizing guinea-pigs or rabbits with toxoid prepared from this material, that they had become more resistant than controls to infections of the bladder by BINGEL'S technique (*Ztschr. f. Hyg. u. Infektionskr*, 1944, v. 125, 110), or to conjunctival infections. *J. W. McLeod*

STENZEL, W. Serologische und toxikologische Untersuchungen der Lipopolysaccharide schleimhautpathogener und -apathogener Shigella-Stammpaare. **[Serological and Toxicological Investigations of the Lipopolysaccharide of Strains of Shigella before and after Loss of Capacity to invade Mucous Membranes]** *Ztschr. f. Hyg. u. Infektionskr.* 1961, v. 147, No. 4, 391–8. [41 refs.]

The strains selected, a Flexner 3 and a Boyd 2 shigella, were passed repeatedly on Endo and Leifson media until they had lost their ability to produce lesions of the guineapig bladder (Bingel's technique) or of the eye. The non-pathogenic strains could not be distinguished from the original one in the case of the Flexner strain either by lipopolysaccharide content, endotoxin (in mouse experiment) or by defect of O-antigen.

In the case of the Boyd strain a partial defect in O-antigen was detected in the non-pathogenic strain.

J. W. McLeod

ŚLOPEK, S. & MULCZYK, M. **Phage Types of *S. flexneri*.** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 3, 417–21.

Using 12 bacteriophages isolated from human and animal faeces the authors examined 2,658 strains of *Shigella flexneri* and were able to classify them into 40 phage types. The distribution of phage types within particular serotypes suggests the possibility of differentiating a number of subtypes in a single serotype. Further studies are in progress to determine how

valuable this phage-typing method will prove to be in epidemiological investigations. *H. J. Bensted*

MULCZYK, M. & LACHOWICZ, T. M. **Preliminary *in vitro* Studies on the Mechanism of Selection among Serological *Shigella flexneri* Types.** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 3, 423–36, 5 figs.

In a previous paper MULCZYK [this *Bulletin*, 1960, v. 35, 927] showed that mouse-passage of a strain of *Shigella flexneri* 1b resulted in the loss of type antigen I and the acquisition of type antigen III without any change in the group antigen make-up. The change in type antigen occurred after 10 passages in mice and with it came the development of resistance to phage F2 to which the original strain was sensitive. It is considered that the results obtained were due to selection of a pre-existing mutant spontaneously formed in the original *Sh. flexneri* 1b population.

The present paper is concerned with *in vitro* studies with the original and the mutant strains on the mechanism of selection. With large inocula of equal amounts of the original I: 3, 4, 6 and the mutant III: 3, 4, 6 into nutrient broth it was found that the first 24 hours subculture contained equal numbers of viable cells of both types as determined by serological tests and phage-sensitivity tests, in the next 24 hours subculture most of the colonies developing on plate cultures from this broth were of the mutant type and further subcultures resulted in the complete emergence of the mutant form as a pure culture. When minimal synthetic medium was used in place of nutrient broth selection was not observed.

Although a satisfactory explanation is not offered it appears that some factor prevents multiplication of the original I: 3, 4, 6 form and it is suggested that this may be due to the release of a latent phage or a colicine agent. The total bacterial increase in the cultures after the first subculture was almost entirely due to the multiplication of the mutant forms.

H. J. Bensted

LACHOWICZ, T. M. & MULCZYK, M. **Genetic Mechanism of the Antigenic Variability of *Shigella flexneri* 1b.** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 3, 437–49. [26 refs.]

More detailed study of the resistance to F2 phage found in mutants of *Shigella flexneri* 1b [see above] shows that these mutants are of 3 types: one shows the loss of type antigen I and the acquisition of type antigen III, the second appears to contain both type antigens I and III and the third has the same antigenic formula as the parent strain—I: 3, 4, 6—but is resistant to phage F2. By the application of the replica method of LEDERBERG and LEDERBERG [this *Bulletin*, 1954, v. 29, 304] it was possible to show that all 3 mutants were present in the population of the parent strain and that this was independent of any action of the phage itself and other tests showed that the 3 mutants occurred in independent clones with different mutation rates. The mutation rate for the mutant showing loss of type antigen I and acquisition of type antigen III was about 4×10^{-7}, for the mutant containing both type antigens (I and III) 8×10^{-8} and for the mutant which had the antigenic structure of the parent but was resistant to phage F2 it was about 8×10^{-8}. Further studies on the selection mechanism are being carried out. *H. J. Bensted*

AKIBA, T., KOYAMA, K., ISHIKI, Y., KIMURA, S. & FUKUSHIMA, T. **On the Mechanism of the Development of Multiple-Drug-Resistant Clones of *Shigella*.** *Japanese J. Microbiol.* 1960, Apr., v. 4, No. 2, 219–27.

This paper is concerned with the transfer of drug resistance from one bacterial species to another by mixed cultivation. Strains of *Escherichia coli* isolated from human faeces and found to be resistant to streptomycin, chloramphenicol, the tetracyclines and sulphonamides, could, if cultivated in the presence of *Shigella flexneri*, previously sensitive to these substances, produce the same multiple-resistant clones of *Shigella*. Similarly a strain of *E. coli* resistant only to streptomycin, for example, when grown with a streptomycin-sensitive *Shigella* strain resulted in streptomycin-resistant clones of the shigella strain but the biochemical and serological properties of the recipient strain remain unchanged. Unlike the results reported by LURIA and BURROUS [this *Bulletin*, 1959, v. 34, 1041] the present findings on the transfer of resistance appeared to be unrelated to the F-factor since the transfer occurred without accompanying unselected markers and the results suggest that the transfer of resistance-factors is similar in mechanism to that of the colicinogenic factor. The authors quote clinical observations in which patients with dysentery excreted, during the acute stage of the disease, drug-resistant *E. coli* and drug-sensitive shigellae but some days later the shigellae were drug-resistant. Furthermore when drug-resistant *E. coli*, as a broth culture, was injected per-anally into patients who were excreting drug-sensitive shigellae subsequent isolations yielded drug-resistant shigellae. *H. J. Bensted*

ISHII, F. **Studies on the Hemolytic Property of *Escherichia coli*.** *Japanese J. Microbiol.* 1960, Apr., v. 4, No. 2, 203–18. [15 refs.]

The author employed the blood agar plate culture and the peptone water culture methods for studying the haemolytic property of a variety of different strains of *Escherichia coli* isolated from man and domestic animals. The blood agar plate method was not reliable for the determination of true haemolysis for approximately half the cultures showing haemolytic activity by this method failed to show haemolysis when tested by the peptone water technique. The strains giving positive results by the latter method were shown to produce a soluble haemolysin which was thermolabile.

Moreover the haemolytic titres were much reduced by high speed centrifugation of the fluid cultures and the property was lost after passage through bacterial filters and treatment by certain chemicals. Strains showing haemolysis by the blood agar plate method were derived from both normal and pathological material but all the strains giving a positive result by the peptone water method, that is to say all those strains producing a soluble haemolysin, were derived from pathological material exclusively and it is suggested therefore that the latter test is suitable for indicating the pathogenicity of a strain of *E. coli*. When the production of soluble haemolysin was examined in relation to the O antigen some degree of correlation was found but there was variation in the haemolytic titres of different strains of the same serotype. Although the author hesitates to call the haemolytic substance an exotoxin he suggests that it could be one kind of a high-molecular zymoprotein. *H. J. Bensted*

SUSSMAN, S. **The Passive Transfer of Antibodies to *Escherichia coli* O111 : B4 from Mother to Offspring.** *Pediatrics.* Springfield, Ill. 1961, Feb., v. 27, No. 2, 308–13. [17 refs.]

The antibody titres in this study were estimated by haemagglutination techniques, trypsinated and untrypsinated red cells being used in comparative tests. There were 27 mothers and their respective infants in the investigation. Sera and colostra of the mothers all contained haemagglutinating antibodies for *Escherichia coli* O 111 and in 19/27 cases the antibody titres of the first day colostrum specimens were higher than the corresponding serum specimens but these fell rapidly during the next 3–4 days. Only 5 of the infants' cord sera showed haemagglutination antibody to *E. coli* O 111. These results were obtained by the more sensitive trypsinated red cell technique and were all low titre antibody. The significance of these findings appears to be very doubtful. *H. J. Bensted*

SNEATH, P. H. A. & LEDERBERG, J. **Inhibition by Periodate of Mating in *Escherichia coli* K-12.** Reprinted from *Proc. Nat. Acad. Sci.* 1961, Jan., v. 47, No. 1, 86–90. [16 refs.]

"Periodate, and to a lesser extent, persulfate and perborate, devirilize the male mating types of *E. coli* K-12. The devirilized cells can still act as females, however, and female mating types are not affected by periodate at the relevant concentrations. Devirilized cells recover their virility after about 2 hours in broth culture. The action of periodate appears to be to prevent the formation of mating pairs of cells, probably by altering the surface properties of male cells. The effect is consistent with an oxidation of glycol links in a polysaccharide on the surface of male cells. Treatment of F^+ cells with periodate also makes them unable to transmit the *F* agent by infection."

ARGENTON, H., BECKER, H., FISCHER, H., OTTO, J., THIEL, R., & WESTPHAL, O. Über die resistenzsteigernde Wirkung von Lipoid A beim Menschen. **[The Effects of Lipid A in Man]** *Deut. med. Woch.* 1961, Apr. 21, v. 86, No. 16, 774–81, 838, 5 figs. [42 refs.]

The English summary appended to the paper is as follows:—

"Lipid A, made of purified coli-endotoxin, was injected intravenously in control persons and patients in doses which would give no or only slight pyrexia (without malaise, headache or limb aches). Invariably there was an increase in segmented leucocytes (2—3 × control values). These leucocytes had a much enhanced power of phagocytosis, due to an increase not in serum opsonins, but in cell performance. The effects of Lipid A were not diminished after repeated injections. Preliminary clinical trials have shown that in certain eye conditions a non-pyrogenic dose of Lipid A influenced the course of the disease as favourable as fever-therapy. In cases of optic neuritis, in which the usual methods of treatment had failed after many weeks, Lipid A produced impressive improvement, which could be substantiated by objective tests."

HAMERS, R. & HAMERS-CASTERMAN, C. **Synthesis by *Escherichia coli* of an Abnormal β-Galactosidase in the Presence of Thiouracil.** *J. Molecular Biol.* London. 1961, Apr., v. 3, No. 2, 166–74, 5 figs. [31 refs.]

TURNER, J. M. & HAPPOLD, F. C. **Pyridoxamine Phosphate-Oxidase and Pyridoxal Phosphate-Phosphatase Activities in *Escherichia coli*.** *Biochem. J.* 1961, Feb., v. 78, No. 2, 364–72, 5 figs. [27 refs.]

WADE, H. E. **The Autodegradation of Ribonucleoprotein in *Escherichia coli*.** *Biochem. J.* 1961, Mar., v. 78, No. 3, 457–72, 14 figs. [36 refs.]

RACHMELER, M., GERHART, J. & ROSNER, J. **Limited Thymidine Uptake in *Escherichia coli* due to an Inducible Thymidine Phosphorylase.** *Biochim. et Biophys. Acta.* 1961, Apr. 29, v. 49, No. 1, 222–5, 2 figs. [12 refs.]

FREDERICQ, P. Recherches sur le déterminisme génétique de la propriété Hfr chez *Escherichia coli*. **[Study of the Genetic Determinism of the Hfr Property in *Escherichia coli*]** *C.R. Soc. Biol.* 1960, v. 154, No. 11, 2146–50.

STRANGE, R. E., DARK, F. A. & NESS, A. G. **The Survival of Stationary Phase *Aerobacter aerogenes* stored in Aqueous Suspension.** *J. General Microbiol.* 1961, May, v. 25, No. 1, 61–76, 11 figs. [38 refs.]

YAGER, R. H., SPERTZEL, R. O., JAEGER, R. F. & TIGERTT, W. D. **Domestic Fowl—Source of High Titer *P. tularensis* Serum for the Fluorescent Antibody Technic.** *Proc. Soc. Exper. Biol. & Med.* 1960, Dec., v. 105, No. 3, 651–4. [12 refs.]

It was found that a single injection of living *Brucella tularensis*, as an intravenous dose of 5×10^6 viable organisms, in various breeds of domestic fowls of 8–10 lb. weight yielded an anti-tularensis serum of greater specificity and higher titre than multiple injections of killed organisms into rabbits or monkeys. Gamma globulin prepared from these sera and conjugated with fluorescein isothiocyanate were tested against a number of different organisms, including the homologous strain of *Br. tularensis*, by the fluorescent antibody technique. At low titre all the globulin preparations showed some cross reactions with certain of the organisms tested, particularly *Pseudomonas spp.* This suggested a specific antigenic relationship between *Br. tularensis* and the strain of *Pseudomonas* since this cross reaction was removed by specific absorption technique. The higher titres of the fowl globulin enabled higher working dilutions to be used than with the monkey or rabbit globulins with consequently an improvement in specificity. *H. J. Bensted*

WILLIAMS, E. **Septicaemia caused by an Organism resembling *Pasteurella septica* after a Dog-Bite.** *Brit. Med. J.* 1960, Dec. 31, 1926–9. [27 refs.]

Septicaemia, proved by 1 positive blood culture out of 3, followed a dog bite of the left foot. The same pasteurella was isolated from the patient's blood and wound and from the dog's mouth. The rarity of pasteurella septicaemias complicating the much more common local wound infections is noted, and the literature on the few reported cases is reviewed. In this particular case the patient was icteric and was ultimately shown at laparotomy to be suffering from post-necrotic cirrhosis. The association of pasteurella septicaemia with cirrhosis of the liver in at least two previously reported cases is noted.

[The organism responsible for the septicaemia in the present case is only tentatively included in the genus *Pasteurella*. It differs in several ways from *P. septica*, especially in its ability to ferment lactose and maltose. H_2S production was not tested although it is useful in characterizing the group. The immunological investigations were devoted largely to showing that the patient had produced antibodies against the homologous strain isolated from the wound and the dog's mouth. The reactions of the patient's serum with known *Pasteurella species* are not recorded and the isolated organism is agglutinated to a titre of only 1 in 20 by specific antiserum.

A mouse inoculated with an unstated dose of the organism by an undisclosed route died in 36 hours but we are not told whether or not this was due to septicaemia. Guineapig inoculation gave a local abcess after a week but rabbit and pigeon were not inoculated.] *Stewart Fletcher*

BAIN, R. V. S. & KNOX, K. W. **The Antigens of *Pasteurella multocida* Type I. II. Lipopolysaccharides.** *Immunology*. Oxford. 1961, Apr., v. 4, No. 2, 122–9, 1 fig. [15 refs.]

THORNE, C. B., MOLNAR, Dorothy M. & STRANGE, R. E. **Production of Toxin *in vitro* by *Bacillus anthracis* and its Separation into Two Components.** *J. Bacteriology*. 1960, Mar., v. 79, No. 3, 450–55.

Anthrax toxin found in plasma of guineapigs dying of anthrax infection was found to contain two components which were separated by ultracentrifugation [SMITH *et al.*, this *Bulletin*, 1957, v. 32, 91]. Although initial attempts failed, toxin production *in vitro* was eventually accomplished when serum was added to the medium [HARRIS-SMITH *et al.*, *ibid.*, 1959, v. 34, 495].

The present workers found that when *B. anthracis* was grown in a Casamino acids medium [THORNE and BELTON, *ibid.*, 1958, v. 33, 180] supplemented with 10% horse serum or 1% gelatin, toxin was produced; but when no protein was added the culture filtrate was non-toxic. It was found that the non-toxic filtrate from the unsupplemented culture contained the same amount of protective antigen as did the toxic filtrates. This paper shows that the anthrax toxin is composed of 2 factors, one of which is the protective antigen and the other is a substance which does not pass through fritted glass filters at *p*H 7·0 in the absence of protein. The addition of serum or gelatin is not required for the production of toxin but does allow the other component to be filtered.

The non-filterable component of the toxin grown in medium without protein was eluted from the filters when they were treated with a 0·1M $NaHCO_3$–NA_2CO_3 buffer at *p*H 9·7. Neither of the components by itself was toxic as shown by a skin reaction in guineapigs or a lethal effect in mice. The toxin was neutralized by an antiserum to the protective antigen. *D. D. Smith*

BONVENTRE, P. F., NORDBERG, B. K. & SCHMITER-LÖW, C. G. **An Autoradiographic Study of Anthrax Infection in the Mouse.** *J. Infect. Dis.* 1961, Mar.–Apr., v. 108, No. 2, 205–12, 6 figs. [14 refs.]

"The whole body autoradiographic method was used for the study of experimental anthrax infection in the mouse. It was found by the degree of radioactivity accumulating in the body after intravenous inoculation of S^{35}-methionine-labelled *Bacillus anthracis* that the lung, liver and spleen were most active in clearing the initial bacteremia. The resurgence of the secondary bacteremia was not demonstrable in the autoradiograms but the possible importance of the lung rather than the liver and spleen in this respect was discussed. The significance of the high degree of radioactivity seen in the kidney and bladder was also discussed. The advantages of the whole body autoradiographic technique for the study of experimental bacterial infections were demonstrated."

BITTNER, J., VOINESCO, Viorica & ANTOHI, S. La sensibilité aux antibiotiques des anaérobies du genre *Clostridium*, déterminée *in vitro* par diffusion circulaire en gélose. [**The Susceptibility to Antibiotics of Anaerobes of the Genus *Clostridium*, as determined *in vitro* by means of Circular Diffusion in Agar**] *Arch. Roumaines Path. Expér. et Microbiol.* 1961, Mar., v. 20, No. 1, 63–76, 11 figs. [32 refs.]

The English summary appended to the paper is as follows:—

"1. The susceptibility of 62 strains belonging to 13 species of the genus *Clostridium* to 17 antibiotics and sulphonamides in various dilutions was investigated by means of a simple method of circular diffusion in agar. This method was devised by one of the authors in 1952 and resembles the method described by CHABBERT in 1951. Both filter paper disks soaked with the antibiotic at the moment they are used and commercial soaked and dried disks may be used.

"On the whole, 5000 determinations have been carried out.

"2. On the whole, the species investigated, i.e. *Cl. perfringens* types A,B,C,D,E,F, *Cl. tetani, Cl. oedematiens, Cl. histolyticum, Cl. septicum, Cl. cochlearium, Cl. chauvoei, Cl. bifermentans, Cl. sordellii, Cl. sporogenes, Cl. fallax, Cl. gigas,* and *Cl. tertium* were found to be susceptible to penicillin, aureomycin, chloramphenicol, terramycin, tetracycline, erythromycin, bacitracin, magnamycin, and not susceptible to nitrofuran, neomycin, streptomycin, polymixin, gramicidin, tryocidin, and tyrothricin.

"The susceptibility to the sulphonamides salvoseptyl and superseptyl displays great variations from one strain to another of the same species as well as from one determination to the other.

"The following are exceptions to the above statements:

"None of the (22) strains of *Cl. tetani* or of the strains of *Cl. histolyticum, Cl. sordellii,* and *Cl. tertium* was susceptible to bacitracin. The 5 strains of *Cl. oedematiens* and 4 out of 5 strains of *Cl. septicum* were susceptible to neomycin.

"3. As a rule, no considerable differences were found to exist between the susceptibilities of strains belonging to the same species, and the order of activity of the antibiotics is more or less the same in all species.

"The most exacting species as regards anaerobiosis are the most susceptible to antibiotics and conversely, the least susceptible ones are the microaerophilic species.

"4. Among the strains investigated, none was found to be resistant to the main antibiotics."

EMMELIN, N. **Supersensitivity of Salivary Gland caused by Botulinum Toxin.** *J. Physiology.* 1961, Apr., v. 156, No. 1, 121–7, 3 figs. [16 refs.]

GOWLAND, G. & WILLIS, A. T. **Resistance of Lysolecithin to the Action of *Clostridium welchii* Alpha-Toxin.** *J. Path. & Bact.* 1961, Apr., v. 81, No. 2, 542–3.

FAGUET, M. La croissance de *Cl. sporogenes* étudiée au microbiophotomètre électronique. I. Actions comparées de Ni++ et de Co++. [**Studies on the Growth of *Clostridium sporogenes*. I. Comparative Activity of certain Cobalt and Nickel Salts**] *Ann. Inst. Pasteur.* 1961, May, v. 100, No. 5, 594–9, 5 figs.

MORTER, R. L. **A Hemolytic Phenomenon in Ewes requiring *Leptospira pomona* Antigen and Antibody.** *Proc. Soc. Exper. Biol. & Med.* 1961, Mar., v. 106, No. 3, 600–603. [13 refs.]

ROBIN, L. A. & MAGARD, H. Contribution au diagnostic bactériologique des méningites à *Listeria monocytogenes.* [**The Bacteriological Diagnosis of *Listeria monocytogenes* Meningitis**] *Ann. Inst. Pasteur.* 1960, Dec., v. 99, No. 6, 905–15. [14 refs.]

This is a study of the laboratory diagnosis of *Listeria monocytogenes* based on experience with 2 adult patients (one with fatal septicaemia and one with meningitis who recovered), and 4 fatal cases of meningitis in infants.

Confusion is likely to arise with *Corynebacteria, Erysipelothrix rhusopathiae* and streptococci A and D. The most useful differential tests are that for catalase which is positive only with corynebacteriae and *L. monocytogenes*; motility in 18-hour cultures in 0·5% glucose broth which differentiates it from corynebacteriae; and Anton's test—production of purulent conjunctivitis in the eye of the guineapig, which is not given by the other bacteria mentioned.

The Listeria are sensitive to sulphonamides and to kanamycin and erythromycin among antibiotics.

J. W. McLeod

ADA, G. L., FRENCH, E. L. & LIND, P. E. **Purification and Properties of Neuraminidase from *Vibrio cholerae*.** *J. General Microbiol.* 1961, Mar., v. 24, No. 3, 409–21, 7 figs. & 1 pl. [21 refs.]

PYE, J. & CURTAIN, C. C. **Electrophoretic, Sedimentation and Diffusion Behaviour of Crystalline Neuraminidase from *Vibrio cholerae*.** *J. General Microbiol.* 1961, Mar., v. 24, No. 3, 423–5, 3 figs. on pl.

GUHA, D. K. & MUKERJEE, S. **Amino-Acid Composition of Phage-Types of *Vibrio cholerae*.** *Ann. Biochem. & Exper. Med.* Calcutta. 1960, Dec., v. 20, No. 12, 349–52. [16 refs.]

BACTERIOPHAGES

HARMEGNIES, J., HAWARI, M. & MUTSAARS, W. Le chauffage des germes et son effet sur la multiplication du phage partiellement inactivé par le formol. **[The Heating of Micro-Organisms and its Effect on the Multiplication of Phage partially inactivated by Formaldehyde]** *Ann. Inst. Pasteur.* 1961, Feb., v. 100, No. 2, 214–31.

When phage φN which had been partially inactivated with formaldehyde was plated on *Escherichia coli* W, more plaques were obtained on plates incubated at 42°C. than at 37°C. It was found that heating the bacteria alone at temperatures above 37°C. for 5 minutes, before mixing them with formolized phage, increased the yield of phage. This phage increase rose with temperature to reach an optimum at 48°C.: most phage was obtained from bacteria which had been incubated at 48°C. for 15 minutes. If these heated bacteria were then incubated at 38°C. in broth before being mixed with formolized phage, the increased yield of phage gradually diminished, though even after 30 minutes at 38°C. heated bacteria still produced more phage than untreated bacteria. Bacteria which had been exposed to small doses of UV light before heating at 48°C. gave rise to as many plaques on infection with formolized phage as heated unirradiated bacteria, but bigger UV doses suppressed the effect of heat (without abolishing the ability to grow phage). Bacteria which were first heated and then irradiated lost the capacity to produce bigger yields of phage. Chloramphenicol added to the bacterial culture before it was heated reduced the yield of phage. Experiments with young and old cultures grown in aerobic and semi-anaerobic conditions indicated that, after infection with formolized phage, the yield of phage was greatest from 29-hour semi-anaerobic cultures incubated at 38°C.

Heating bacteria did not increase the yield obtained from phage inactivated by UV light, or heat, or by mercuric chloride, phenyl isocyanate or nitrogen mustard. The heating effect was only observed with phage inactivated by aldehydes (*e.g.* formaldehyde, glyoxal, acrolein).

The authors put forward no theory which explains all these results. They point out that the effect of heat could be explained if an enzyme which inhibits the multiplication of formolized phage is destroyed at 48°C., and if its activity is restored, or more of it is synthesized, when the heated culture is held at 38°C. before plating. However, UV irradiation would be expected to inhibit the synthesis of the enzyme and therefore to increase the production of phage even more, but in fact large UV doses were found to reduce the heating effect and to decrease the yield of phage.

[See also this *Bulletin*, 1960, v. 35, 705.]

Janice Taverne

HUDEMANN, H. Fundorte und Bedeutung von Typhus-Vi-Phagen in der Natur. **[Habitat and Significance of *Salm. typhi* Vi-Phages in Nature]** *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 2, 234–40, 1 fig.

The material brought under investigation consisted of (a) human stools obtained from patients with enteric infection, carriers of such infection and others; (b) animal faeces obtained from the carcases at the slaughterhouse; (c) sewage water both raw and in various stages of purification; (d) a variety of foodstuffs.

The centrifugal supernatant from washings or suspensions of various materials was heated at 56°C., and then tested for phage activity on Vi typhoid strains and also on a variety of Vi free strains including *Salm. typhi*, other Salmonellae, *Shigella*, *Escherichia* and *Proteus* strains. Only phage active on the Vi typhoid culture but not on any of the Vi free strains or still capable of acting on the former after absorption by the latter were accepted as Vi phages.

The general conclusion reached from these investigations was that the presence of Vi typhoid phage is a valuable evidence of pollution by human faeces but not evidence for the presence of typhoid infection. The Vi phage was found in 6·7% of patients infected with *Salm. typhi* but also in 1·8% of patients free from such infection.

J. W. McLeod

WALLMARK, G. & FINLAND, M. **New Phages Active against Staphylococci that are resistant to the Conventional Phage Set.** *Proc. Soc. Exper. Biol. & Med.* 1961, Jan., v. 106, No. 1, 73–8.

By cross-culture of 108 strains of staphylococci that were untypable with the standard set of phages, even when used 1.000 times stronger than the routine test dilution, 5 new phages were isolated; 2 other new phages were isolated from the original staphylococcus cultures. The 7 phages were propagated and characterized by their activity on the standard test strains; 2 were found to be very similar and 1 of these was therefore omitted from further tests.

Of 158 staphylococci untypable with the standard phages 116 (73%) were lysed by 1 or other of the 6 new phages, 1 (A) lysing 44% of them and 2 others (B and F) 7% and 6% respectively. Phage F is similar to phage 81. Phage A only lysed a small number of otherwise typable staphylococci—2 of type 47/53/83 and 8 of type 53.

R. E. O. Williams

UYEDA, S. & ITO, Y. Deux souches de mycobactériophages récemment isolées et leur action sur des micro-colonies d'une mycobactérie saprophyte. **[Two Strains of Mycobacteriophages recently isolated and their Activity on the Micro-Colonies of a Saprophytic Mycobacterium]** *Ann. Inst. Pasteur.* 1961, May, v. 100, No. 5, 681–4, 1 text fig. & 8 figs. on pl.

ARONSON, A. I. **The Inhibition of Bacteriophage Protein Synthesis by 5-Fluorouracil.** *Biochim. et Biophys. Acta.* 1961, Apr. 29, v. 49, No. 1, 89–97, 2 figs. [20 refs.]

——. **The Effect of 5-Fluorouracil on Bacterial Protein and Ribonucleic Acid Synthesis.** *Ibid.*, 98–107, 10 figs. [16 refs.]

BERTANI, L. Elizabeth. **Levels of Immunity to Superinfection in Lysogenic Bacteria as affected by Prophage Genotype.** *Virology.* New York. 1961, Mar., v. 13, No. 3, 378–80, 1 fig.

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

COOPER, P. D. **A Chemical Basis for the Classification of Animal Viruses.** *Nature.* 1961, Apr. 22, v. 190, 302–5. [40 refs.]

A classification of animal viruses which might be extended to embrace bacterial and plant viruses is based on 3 criteria: nucleic acid content, ether-sensitivity and size. The primary division is into deoxyviruses (DNA) and riboviruses (RNA)—this distinction can most readily be made either by the preparation of infective nucleic acid which can then be treated with nucleases or by testing for inhibition of growth by 5-fluorodeoxyuridine which affects growth only of deoxyviruses. The second criterion distinguishes those viruses of which lipid components are essential for infectivity. The ether-resistant viruses have a strong and regular lattice-like (clathrate) substructure (clathroviruses) whereas the sensitive viruses are less rigid (lipoviruses). A detailed classification is tabulated with additional grouping by size. Certain growth properties are correlated with this classification: deoxyviruses (*e.g.* vaccinia, herpes, adenovirus) are slow to mature and to be released, and form marked inclusion bodies while riboviruses mature faster and do not form marked inclusions. Liporiboviruses (*e.g.* vesicular stomatitis, influenza, western equine encephalitis) probably mature at the cell wall while clathroriboviruses (*e.g.* polio, encephalomyocarditis, foot-and-mouth) mature probably in the cytoplasm.

C. E. Gordon Smith

SPIRIN, A. S. **The Chemical Nature of Viral Infectivity.** *Russian. Rev. Biol.* London. 1961, Apr., 245–58. [Numerous refs.] [Translated from Russian Uspekhi Sovremennoi Biol. 1960, Nov.–Dec., v. 50, No. 3.]

A review of the subject.

COLLIER, L. H. **Experiments with Trachoma Vaccines. Experimental System using Inclusion Blennorrhoea Virus.** *Lancet.* 1961, Apr. 15, 795–800, 4 figs. [21 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 953.]

SHUBLADZE, A. K. & MAYEVSKAIA, T. M. **Study of Neurotropic Viruses in Tumours grown in Fertile Eggs.** *Problems of Virology.* London. 1960, v. 5, No. 4, 458–65. [13 refs.] [Translated from Russian.]

The Crocker sarcoma and the Brown-Pearce carcinoma were grown on the chorioallantoic membrane of 10–11-day eggs. Most experiments were done with the former but similar results were obtained with both. The tumours when grown for 5–7 days were directly inoculated with mouse-brain virus. Tissues from eggs with and without tumours were titrated for virus in mice after 1–4 days.

4 strains of herpes virus were studied. 3 of them grew well in the tumour (titres 4·0–4·7 log). The exception grew better in the chorioallantoic membrane in control eggs than in tumour eggs: the others grew equally in the chorioallantoic membrane in both types of egg. Little virus was found in the allantoic fluid and none in the brain or body of the embryo.

2 strains of tick-borne encephalitis virus were studied. Both grew well in the tumours and also in all the tissues of both control and tumour eggs. Eastern and western encephalitis viruses were compared. Both grew well both in the tumours and in the chick embryo tissues. A "human encephalomyelitis virus" [the nature of which is not clear] was also studied: it grew in the tumours and in tissues of tumour eggs but not in the control eggs except in the chorioallantoic membrane rather late.

4 strains of hepato-encephalotropic viruses were studied. All grew in the tumour and chorioallantoic membrane and all except the Motol strain grew well in the chick embryo brain and body.

C. E. Gordon Smith

MAHNEL, H. & HERRLICH, A. Zur Züchtung des Variola-und Alastrimvirus in bebrüteten Hühnerei. **[The Propagation of Variola and Alastrim Virus in the Embryonated Chicken Egg]** *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 2, 137–49, 1 fig. [23 refs.]

In this work the authors used 7 strains of smallpox virus, one of alastrim and one of vaccinia. Most of the work with smallpox virus was done with a strain called "Bombay 1958". They found that incubation of infected chick embryos at 39°C. caused a reduction in virus multiplication. Results are given of titrations at 35°C. and 39°C. of 2 unspecified virus suspensions: one had its titre reduced about 6-fold at 39°C., the other about 500-fold. They also found differences in the degree of generalization. Throughout the dose range 1 to over 100 ID50 vaccinia virus showed maximum generalization. Variola virus showed regularly increasing generalization with increasing dose. Alastrim virus showed mild to moderate generalization throughout the dose range. After inoculation of 1000 ID50 4% of embryos infected with vaccinia virus survived at the 4th day. After similar doses of variola and alastrim viruses the survivals on the 7th day were 52% and 75% respectively. After inoculation of 1000 ID50 of Bombay 1958 virus there were 58% survivors after the 5th day of incubation at 35°C.; 90% at 37°C. and 80% at 39°C. The authors suggest that their findings may be used to distinguish between variola and alastrim virus strains.

[The method described by NIZAMUDDIN and DUMBELL [this *Bulletin*, 1961, v. 36, 607] is much simpler, gives quite clear-cut answers and is altogether more elegant.] *Colin Kaplan*

HANAFUSA, H., KAKU, H., HANAFUSA, T. & KAMAHORA, J. **Chromatography of Vaccinia Virus.** [Correspondence.] *Biken's J.* Osaka. 1960, Dec., v. 3, No. 4, 357–8, 1 fig.

HANAFUSA, T. **Alteration of Nucleic Acid Metabolism of Host Cells by Active and Inactivated Forms of Vaccinia Virus.** *Biken's J.* Osaka. 1960, Dec., v. 3, No. 4, 313–27, 7 figs. [29 refs.]

MAHNEL, H. Tierexperimentelle Untersuchungen mit Vakzine-Antigen. 1. Mitteilung: Der Einfluss einer Vorimpfung mit inaktiviertem Antigen auf die nachfolgende Vakzineinfektion des Kaninchens. **[Animal Studies with Vaccinia Virus. 1. Effect of Previous Inoculation with Inactivated Virus on Subsequent Challenge with Potent Vaccine in Rabbits]** *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 4, 529–39, 2 figs. [11 refs.]

Vaccinia virus suspensions were prepared from chick embryo chorio-allantoic membrane, dermal pulp and tissue culture. The suspensions were exposed to 0·03% formalin at 4°C. and tested daily for residual infectivity. They were regarded as non-infectious when an undiluted inoculum gave no lesions in chick embryo, and when a 10-fold concentration of the preparation was similarly inactive. Inactivation was complete within 11 days as a rule.

Rabbits were injected intramuscularly with one dose of the non-infectious materials and challenged at various periods up to 28 days by vaccination with a known potent smallpox vaccine. The degree of immunity depended on the time between injection and challenge rather than on the titre of virus before formalization. [This point is not as clearly shown as it might have been, as the author records only one experiment on these lines.] All of the 18 preparations used induced a good level of immunity, judged by the response of test rabbits to challenge. *Colin Kaplan*

SZATHMÁRY, J. **Studies on the Non-Specific Inhibition by some Body Fluids against Vaccinia Haemagglutination.** *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 4, 540–49. [33 refs.]

Non-specific inhibitors of vaccinial haemagglutination are described in various human body fluids. The non-specific inhibitors could be distinguished from specific inhibitors (*i.e.*, antibody) by a greater degree of heat sensitivity. They were shown to act directly by combining with haemagglutinin, not with the red cells. They were generally destroyed by trypsin and adsorbed by kaolin. Treatment with these 2 substances had no apparent effect on specific antibodies. *Colin Kaplan*

KAPLAN, C. **The Antigenicity of γ-Irradiated Vaccinia Virus.** *J. Hygiene.* 1960, Dec., v. 58, No. 4, 391–8, 1 fig. [15 refs.]

The Lister Institute vaccine strain was exposed to gamma rays from a cobalt-60 source. Suspensions of virus partially purified by centrifugation and diluted in phosphate citric acid buffer to a titre of 10^7 pock-forming units per ml. were completely inactivated in terms of egg infectivity by doses of 6–8 × 10^5 rad. After subcutaneous inoculation of rabbits, one batch of irradiated material produced both circulating antibody and resistance to challenge by scarification, one batch gave resistance to challenge without demonstrable antibody rise, and two batches were not immunogenic.

Attempts to work with freeze-dried virus preparations were less successful, and even doses of 11 × 10^6 rad. from the cobalt-60 source failed to give complete inactivation. It is uncertain whether this represents a true heterogeneity of the virus population, or is caused by physical factors such as the protective effects of the peptone used in the freeze-dried preparation [see also this *Bulletin*, 1956, v. 31, 1049]. *Derek Hobson*

WHEELER, C. E., HARVIE, E. J., Jr. & CANBY, C. M. **The Effect of Hydrocortisone on the Production of Herpes Simplex Virus in Tissue Culture.** *J. Investigative Dermat.* 1961, Feb., v. 36, No. 2, 89–97, 4 figs. [32 refs.]

"1. The amount of herpes simplex virus produced in HeLa cultures under maintenance conditions was not

influenced by the presence of hydrocortisone in the medium in amounts of 1, 5 and 10 micrograms per ml.

"2. Hydrocortisone in the maintenance medium had a pronounced effect in delaying and decreasing 'non-specific' degenerative changes of HeLa cell cultures under the conditions of this study."

SCHMIDT, J. R. & RASMUSSEN, A. F., Jr. **The Influence of Environmental Temperature on the Course of Experimental Herpes Simplex Infection.** *J. Infect. Dis.* 1960, Nov.–Dec., v. 107, No. 3, 356–60. [20 refs.]

When groups of mice were maintained in an environmental temperature of 2°, 24° and 37°C. for a week before and 3 weeks after intracerebral inoculation with a given dose of herpes simplex virus, the percentage mortality was the same for mice kept at 2° and 24°C., but it was lower for those kept at 37°C. The brains from infected mice maintained at 37°C. also contained less virus than brains from mice in the other 2 groups. However, the rate of antibody formation against formolized virus and the degree of protection attained was the same in mice held at 37°C. as at 24°C.

The authors consider it unlikely that the lower mortality at the higher temperature was due to heat inactivation of the virus in the body, and their results appear to exclude the possibility of earlier neutralization since antibody production was not accelerated at 37°C. They can only suggest that the altered metabolism of the mice at 37°C. may indirectly reduce the multiplication of virus in the same way that the multiplication of influenza virus is reduced in animals gaining weight more slowly than normal [KALTER *et al.*, this *Bulletin*, 1951, v. 26, 1036]. They point out the paradox that raised environmental temperature should moderate the course of herpes infection of mice while many of the factors (such as fever) which incite the appearance of lesions in the human skin are associated with raised temperature. *Janice Taverne*

NII, S., KAMEYAMA, S., KATO, S. & KAMAHORA, J. **A Study of Herpes Simplex Virus Infection of FL Cells using Autoradiography.** [Correspondence.] *Biken's J.* Osaka. 1960, Dec., v. 3, No. 4, 355–6, 2 figs. on pl.

HOGGAN, M. D., ROIZMAN, B. & ROANE, P. R., Jr. **Further Studies of Variants of Herpes Simplex Virus that produce Syncytia or Pocklike Lesions in Cell Cultures.** *Amer. J. Hyg.* 1961, Jan., v. 73, No. 1, 114–22, 10 figs. (6 coloured on pl.).

One variant (mP) of herpes simplex virus produced microplaques in FL human amnion cells grown in the presence of herpes antibody; it did not cause the formation of giant cells but only clumps of single rounded cells. Another variant (MP) produced macroplaques, each consisting of a clear central area surrounded by a large syncytium. The 2 strains were indistinguishable by neutralization tests done both with immune serum from rabbits and serum from people with recurrent herpes infections. Infected cells stained with acridine orange or with haematoxylin and eosin looked the same with both strains, except for the presence of numerous nuclei in cells infected with MP. Infected cells stained with fluorescein-labelled antibody showed accumulation of antigen in the cytoplasm around the nucleus with both strains, but in cells infected with the MP variant fine fluorescent cytoplasmic processes could be seen emanating from the syncytia and connecting with other syncytia or with uninfected cells. The only other difference observed between the 2 variants was that on serial passage in cell cultures containing antibody, cultures infected with mP virus usually survived while those infected with MP virus invariably degenerated, although enough antibody to neutralize 99·99% of the virus produced was present in the medium.

The authors "are tempted to postulate" that the greater ability of the MP strain to spread directly from cell to cell may be related to the formation of the cytoplasmic processes described, the virus passing along the "corridors" to adjacent cells being inaccessible to antibody, and that the enlargement of these corridors leads to the formation of a syncytium.

Janice Taverne

CANTELL, K. **Stability of Mumps Virus at +35°C.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, No. 3, 309–16, 2 figs. [13 refs.]

The author has investigated the rate of heat inactivation at 35°C. of the Enders and Habel Strains of mumps virus, and also of 2 strains isolated in Finland. Infected allantoic fluid of *p*H 7·5–8·0 containing the virus was kept at 35°C. and the haemagglutinin and infectivity titres were determined in samples removed at intervals up to 4 months. The rate of decrease in infectivity was similar for all strains, and had a mean half-life of 7·3–8·3 hours. The haemagglutinin titre of the Habel and 1 Finnish strain fell to zero within 3–4 weeks, whereas the other 2 strains showed no fall in titre for at least 5 weeks. It is suggested that the difference in stability of the haemagglutinin might be useful as a marker for mumps virus. *D. J. Bauer*

CANTELL, K. **Role of Inhibitors in Hemagglutination Behaviour of Mumps Virus. Further Studies.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, No. 3, 317–25, 4 figs. [19 refs.]

Allantoic fluid containing the Enders strain of mumps virus agglutinated chick, guineapig and human red cells at 4°, 21° and 37°C., but failed to agglutinate cat red cells, and agglutinated mouse red cells only to low titres. When the virus was purified by centrifugation, however, it agglutinated mouse red cells to nearly maximum titres, and agglutinated cat red cells at 4° and 21°C. but not at 37°C. In similar experiments with the Habel strain of mumps virus the crude preparation agglutinated fowl and guineapig but not human, mouse or cat red cells, whereas the purified

preparation agglutinated human and mouse but not cat red cells. The Enders strain purified by centrifugation and subjected to ultrasonic disintegration agglutinated the cells of all species, although somewhat lower titres were obtained with mouse and cat cells. The change in behaviour of the strains of mumps virus was ascribed to the removal of inhibitors [see also this *Bulletin*, 1961, v. 36, 201] and the results indicate that the haemagglutination spectrum is not a reliable criterion for distinguishing between strains.

D. J. Bauer

Sokol, F., Blaskovic, D. & Rosenberg, M. **Subunits of Myxoviruses. I. Treatment of Newcastle Disease, Para-Influenza 1 and Mumps Viruses by Ether.** *Acta Virologica.* Prague. 1961, Mar., v. 5, No. 2, 65–77, 10 text figs. & 2 figs. on 3 pls. [17 refs.]

Newcastle disease virus (NDV), Sendai virus (parainfluenza 1) and mumps virus grown in eggs were purified by ultra-centrifugation and treated repeatedly with ether at room temperature. The material obtained was characterized by its ability to haemagglutinate fowl and guineapig cells, by electron microscopy of shadowed preparations, by ultraviolet absorption spectroscopy and by electrophoresis. Treated NDV was apparently split into smaller haemagglutinating subunits and contained particles 30 $m\mu$ in diameter and filamentous structures. Electrophoresis of treated NDV revealed 2 components. The authors suggest that one may be haemagglutinin and the other nucleoprotein. The other 2 viruses were less affected by ether and less thoroughly studied. *D. A. J. Tyrrell*

Brown, N. K. **Selective Viral and Rickettsial Serum Antibody Absorption by a Chromatographic Column.** *Science.* 1961, Feb. 3, v. 133, 331–2.

"Serum antibodies behave as cations at neutral *p*H and thus have low affinity for cellulose anion-exchange columns. Antigens of small size derived from adenovirus, influenza virus, and typhus rickettisae, however, readily adsorbed to such columns. These adsorbed antigens specifically removed antibodies from antisera. This simple method permits antibody absorption by antigens ordinarily sedimented with difficulty."

Akao, Y., Matsui, T., Sano, R., Shimojo, H., Sugiura, A. & Enomoto, C. **Studies of Myxovirus Infection in Pigs—Antibody in Swine Sera against Myxoviruses.** *Bull. Inst. Pub. Health.* Tokyo. 1960, Mar., v. 9, No. 1, 27–34, 1 fig. [12 refs.]

Sera were collected from pigs killed at slaughterhouses in Tokyo and Osaka before (1956 and early 1957) and during the epidemic of Asian (A2) influenza (August 1957 to February 1958). The sera contained non-specific inhibitors of haemagglutination against influenza A2 virus which could be removed by treatment with periodate but not with RDE. Sera were tested for antibody by haemagglutination-inhibition (HI), complement-fixation (CF) (with V and S antigens) and flocculation. No antibody against Asian influenza (by HI and CF) was found in sera collected before the epidemic or in 427 collected during the epidemic although there were low levels of antibody against swine influenza in 9% and against HVJ [haemagglutinating virus of Japan also known as Sendai or parainfluenza virus type I]. It is concluded that swine played no part in the epidemiology of Asian influenza in Japan. *D. A. J. Tyrrell*

Ishida, N. & Osato, T. **Initial Reactions during Influenza A Virus Invasion into L Cells. Second Report: Growth Characteristics of Myxoviruses in Tissue Culture.** *Tohoku J. Exper. Med.* 1960, Dec. 25, v. 73, No. 1, 46–55, 1 fig. [18 refs.]

Influenza A virus (PR8 strain) was grown on chorioallantoic membrane cultures and labelled with ^{32}P. It was purified by adsorption, elution and centrifugation and mixed with a suspension of Earle's L cells in phosphate buffered saline. A little of the radioactivity left the fluid phase of the mixture but the haemagglutinin activity increased, especially when measured with guineapig cells (from 512 to 1510). The haemagglutinin activity could be adsorbed to red cells but not completely deposited by centrifugation at 26,000 g for 1 or 2 hours. A proportion of radioactivity could not be adsorbed to red cells and also treatment with ether at 37°C. extracted more radioactivity from the fluid phase than from the control virus preparation. The authors conclude that in the system studied virus disintegrated at the cell surface possibly owing to the cell's proteolytic activity and that some haemagglutinin particles were released into the medium. [As the authors point out, normal virus multiplication does not occur but non-infectious haemagglutinin is produced. It is therefore conceivable that the interesting phenomena they observed do not always occur when a myxovirus meets a fully susceptible cell.] *D. A. J. Tyrrell*

Hosaka, Y., Hosokawa, Y. & Fukai, K. **Estimation of Particle Weights of Myxovirus Antigens by the Gel Diffusion Technique.** [Correspondence.] *Biken's J.* Osaka. 1960, Dec., v. 3, No. 4, 351–3, 1 fig.

Schmidt, B., Grossgebauer, K. & Hartmann, D. Über die Enzymaktivität äthergespaltener Influenzaviren und ihren Einfluss auf unspezifische Serum-inhibitoren. **[The Enzyme Activity of Influenza Viruses treated with Ether and their Influence on Unspecific Serum Inhibitors]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Nov., v. 120, No. 4, 238–48, 2 figs. [23 refs.]

The A_2/Singapore/1/57, PR8 and Lee strains of influenza virus in the form of infected allantoic fluid were

shaken with an equal volume of ether at room temperature for 100 hours; the aqueous phase was then recovered and the dissolved ether was allowed to evaporate. In haemagglutination tests with human red cells it was found that the virus treated with ether still retained enzymatic activity, since it would adsorb onto red cells and elute from them, and red cells exposed to the action of the virus could not be agglutinated by it a second time and became panagglutinable. The ether treatment did not abolish the ability of Lee virus to inactivate the unspecific inhibitor present in normal guineapig serum. *D. J. Bauer*

HERZBERG, K. & VANEK, E., with the assistance of Gertrud LÜCK & Ingeborg HARBRECHT. Vergleichende Mäuse-Immunisierungen mit zwei Influenza-A_2-Adsorbat-Impfstoffen. [**Comparative Immunization of Mice with Two Adsorbed Influenza A_2 Vaccines**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 147, No. 2, 133–43. [24 refs.]

An investigation has been made of the immunizing effect in mice of 2 influenza vaccines prepared from the A_2/Singapore 1/57 strain of virus. One vaccine was a commercial preparation of virus grown in eggs and adsorbed on gamma-aluminium oxide, and containing also the A_2/Berlin 18/57 and PR8 strains; the other vaccine was prepared by the authors from virus grown in mouse lung by adsorption on aluminium hydroxide.

Approximately 1,000 mice were immunized with the vaccines given intraperitoneally in 1–3 doses at intervals of 3–4 weeks; the degree of immunity produced was determined 4–8 weeks after the last dose of vaccine by intranasal challenge and serological methods. The results are presented in a series of tables, which show that the immunizing power of the vaccine adsorbed on gamma-aluminium oxide was inferior to that of the vaccine adsorbed on aluminium hydroxide, and that more than 1 dose was necessary in each case for the production of a satisfactory degree of immunity. *D. J. Bauer*

LINK, F., BLASKOVIC, D. & RAUS, J. **Studies on the Effect of Antiviral Substances on Experimental Virus Infections. I. The Effect of Urethane on Influenza Virus Infection.** *Acta Virologica.* Prague. 1961, Mar., v. 5, No. 2, 86–90, 2 figs.

The ID50 of influenza A1 for tissue cultures containing 4·2% or 2·1% urethane was more than 10^4-fold greater than for cultures containing no urethane. Mice were given one dose of 0·1 ml. of 25% urethane at the time of intranasal administration of a large dose of virus. They died (50% mortality) at 6·8 days after infection instead of 4·0 days as in the controls. Animals given 2·5% urethane daily died at 5·4 days. These differences were apparently statistically significant, though animals dying 1 or 2 days after the large dose were excluded from the calculations. A few mice survived. The authors intend to study the matter further. *D. A. J. Tyrrell*

ISHIDA, N. & HOMMA, M. **A Variant Sendai Virus, Infectious to Egg Embryos but not to L Cells. Third Report. Growth Characteristics of Myxoviruses in Tissue Culture.** *Tohoku J. Exper. Med.* 1960, Dec. 25, v. 73, No. 1, 56–69, 6 figs. [21 refs.]

Sendai virus, a strain of parainfluenza I, was propagated in chick embryos and inoculated into bottle cultures of L cells. The cytopathic effect and the yield of haemagglutinin were found to be roughly proportional to the amount of virus inoculated when this was less than about 10^7EID50. Detailed growth curves were carried out. In the cellular phase complement-fixing (CF) antigen was detected at 6 hours, haemadsorption at 7 hours, haemagglutinin (HA) at 8 hours and new infectious activity at 10 to 14 hours. The cytopathic effect began at 14 hours. HA was released into the medium at about 18 hours. The virus produced was capable of infecting chick embryos but not tissue cultures of L cells and the authors consider this to be a kind of host-controlled variation. The only other differences which they detected when comparing this virus and that produced by chick embryo cells were a great reduction in the capacity to haemolyse and a slightly reduced rate of sedimentation in the ultracentrifuge.

[The authors have defined a virus host cell system which might well be useful for a number of different sorts of experimental studies.] *D. A. J. Tyrrell*

MASON, E. J. & KAUFMAN, N. **The Persistent Production of Small Quantities of Infectious Newcastle Disease Virus in Grossly Unaltered L and U_{12} Strain Cells.** *J. Immunology.* 1961, Apr., v. 86, No. 4, 413–20, 1 fig. [12 refs.]

MASON, E. J. & KAUFMAN, N. **Factors affecting the Cytotoxic Reaction between Newcastle Disease Virus and Cells *in vitro*.** *Brit. J. Exper. Path.* 1961, Apr., v. 42, No. 2, 118–30, 1 fig. [31 refs.]

GRESSER, I. & ENDERS, J. F. **A Note on the Presence of Inclusion Bodies in Dividing Human Kidney Cells infected with Croup-Associated Virus.** *Virology.* New York. 1961, Mar., v, 13, No. 3, 370–72, 7 figs.

GREEN, M. & DAESCH, Geraldine E. **Biochemical Studies on Adenovirus Multiplication. II. Kinetics of Nucleic Acid and Protein Synthesis in Suspension Cultures.** *Virology.* New York. 1961, Feb., v. 13, No. 2, 169–76, 6 figs. [18 refs.]

Since the physiological state of cells in monolayers is variable, exponentially growing KB cells in suspension were used in this study. $1·5 \times 10^5$ cells per ml. were infected with 30–100 plaque-forming units (PFU) of type 2 adenovirus per cell. Measurements of virus adsorption, infective centre formation and surviving cells indicated that probably all cells were infected 1

hour after the addition of virus. Intracellular virus was first detectable at 14 hours when 15 PFU of virus per cell were found. Between 14 and 24 hours the amount of virus increased exponentially to 2,000 PFU per cell and levelled off at 4,000–10,000 PFU per cell at about 36 hours. At this time extracellular virus was less than 10% of the intracellular virus. Infected cells were larger than uninfected cells and their dry weight was double that of uninfected cells at 36 hours after infection. The total amounts of protein, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) synthesized in control and infected cultures were similar. However, uninfected cells multiplied while infected cells did not; measurement of cell protein, DNA and RNA for the same number of cells in control and infected cultures showed increases in these constituents in the infected cultures. Thus, there were significant increases 12 hours after infection and at 36 hours the total amounts of protein, DNA and RNA synthesized by 10^6 were about 500, 12 and 30 μgm. respectively.

The authors calculated that if each cell yielded 10,000 virus particles then 10^6 cells would provide a total of only 1·5 μgm. of virus. Some of the discrepancy between this virus mass and that of the synthesized polymers may be due to the inefficiency of the plaque assay. Until this point is determined and until the chemical composition of the virus is known "it will be difficult to assign a definite role to the polymer synthesized during virus infection".

[Part I (*Virology*, 1959, v. 9, 343) was noticed by title in this *Bulletin*, 1960, v. 35, 313.]

D. Taylor-Robinson

KLEIN, M., ZELLAT, J. & MICHAELSON, T. C. **A New Bovine Adenovirus related to Human Adenovirus.** *Proc. Soc. Exper. Biol. & Med.* 1960, Nov., v. 105, No. 2, 340–42, 1 fig.

The authors have previously reported the isolation of a bovine adenovirus [KLEIN *et al.*, this *Bulletin*, 1960, v. 35, 513] and now report the isolation of another bovine strain. In June 1956 this strain was isolated in freshly trypsinized calf kidney cells from the faeces of a calf that was apparently well; paired sera showed a rise in neutralizing antibody to the virus. Identification of the agent as an adenovirus was based on the presence of characteristic intranuclear inclusion bodies and the presence of the group-specific complement-fixing antigen. Rat and mouse red blood cells were agglutinated by the newly isolated strain. By contrast, the initial bovine isolate agglutinated only rat cells. Further, there was no cross reaction between the 2 strains in neutralization tests with immune rabbit serum. The new bovine strain differed from human strains since it did not grow in HeLa or monkey kidney cells and was not neutralized by antisera against human types 1 to 7 [not tested against the other human type antisera]. However, it was recognized as being related to some human virus since 100 tissue culture doses (TCD) of the bovine virus were neutralized by a 1 in 40 dilution of human gamma globulin, and furthermore 100 TCD of virus were neutralized by 9 of 50 adult sera. *D. Taylor-Robinson*

JOHNSON, K. M., BLOOM, H. H., ROSEN, L., MUFSON, M. A. & CHANOCK, R. M. **Hemagglutination by Coe Virus.** *Virology*. New York. 1961, Mar., v. 13, No. 3, 373–5.

COOPER, P. D. **An Improved Agar Cell-Suspension Plaque Assay for Poliovirus: some Factors affecting Efficiency of Plating.** *Virology*. New York. 1961, Feb., v. 13, No. 2, 153–7, 2 figs.

A method for performing plaque assays of poliovirus is described in detail. Cells in suspension in agar are used rather than monolayers as has been previously described by COOPER (*Virology*, 1955, v. 1, 397). The following modifications of the usual technique increased poliovirus efficiency of plating with ERK cells: use of agar cell suspensions rather than monolayers; increase in calcium concentration from 1·5 mM to 7·5 mM; omission of neutral red.

Other modifications were more marginal in effect. These were: tetrazolium staining (COOPER, *Virology*, 1959, v. 7, 469); pretesting of serum and agar for antiviral and toxic effects; use of galactose instead of glucose, a change which allows the omission of bicarbonate and a gassed incubator; treatment of virus suspension with 2 mgm./ml. of sodium deoxycholate; use of 4-inch Petri dishes (rather than 3-inch) to allow larger plaque numbers to be counted without overcrowding; a new series of supplements to the medium are listed. It was found that adsorption time in suspension had little effect in the range 5–180 minutes nor had *p*H in the range 6·8–7·8. The number of cells could be varied from 4,000,000 to 20,000,000 also without effect. The cell suspension method has many virtues: the titres are higher; fewer cells are required, at least with ERK [formerly the large number of cells required has seemed a severe disadvantage of Cooper's method for most workers]; cells are always readily available. It was found that cells could be stored in suspension in a "conservator" for 1–4 days. Cells were stirred in suspension (1 to 2 $\times$ 10^6 per ml.) in galactose-containing medium gassed with air and maintained at 28–32°C. *A. J. Beale*

SALZMAN, N. P. & SEBRING, E. D. **The Source of Poliovirus Ribonucleic Acid.** *Virology*. New York. 1961, Feb., v. 13, No. 2, 258–60. [10 refs.]

Purified poliovirus was used to infect HeLa cells pretreated with labelled uridine and adenine. The pool of acid-soluble nucleotides, cellular and viral RNA were analysed at intervals after infection. It was concluded that the acid-soluble pool was the major source of viral RNA. The cells at the time of infection already contain the RNA and protein precursors necessary for virus synthesis [see also this *Bulletin*, 1956, v. 31, 1270]. *A. J. Beale*

DUBES, G. R. & KLINGLER, E. A., Jr. **Facilitation of Infection of Monkey Cells with Poliovirus "Ribonucleic Acid".** *Science*. 1961, Jan. 13, v. 133, 99–100, 1 fig.

The infectivity titre of RNA extracted from poliovirus by cold phenol treatment is approximately 10^{-6}

that of intact poliovirus. This titre discrepancy can be diminished to the region of 10^{-3} by 2 treatments. (i) Use of a poorly soluble substance to facilitate infection. $CaHPO_4 \cdot 2H_2O$ is one such substance which adsorbs approximately 50% of the poliovirus RNA. (ii) Depletion of the host cells of calcium. Great care is needed to keep the conditions optimal when titrating RNA, otherwise the concentration of the facilitating substance rather than the RNA may well be measured. The tonicity of the saline solution used for the RNA and the cells is also important. If RNA is in a hypotonic solution, peak numbers of plaques are obtained in cells in hypotonic media. If the cells are isotonic, more plaques occur with RNA in hypo- or isotonic solution than in hypertonic solution.

[Other workers have found that RNA in molar NaCl produces more plaques, probably because of an effect of the hypertonic salt solution on the cells.]

A. J. Beale

BALAIAN, M. S. **The Use of the Precipitation Test in Poliomyelitis. I. Preparation of Precipitating Antigens and Use of a Micromethod of Precipitation in Agar Gel.** *Problems of Virology.* London. 1960, v. 5, No. 3, 324–31, 2 figs. [Translated from Russian.]

The successful preparation of antigens for poliovirus precipitin tests in agar is described. The pervaporation technique of POLSON and HAMPTON [this *Bulletin,* 1958, v. 33, 84] was used, followed by centrifugation. During this process approximately 80% of the infectivity was lost but satisfactory antigens were made. High titre virus suspensions (10^9 PFU per ml. or more) were also made by using minimal quantities of fluid to harvest the virus released by the cells. Such high titre virus fluids gave less antigen than concentrates of the same infectivity titre. Other methods of virus concentration gave less satisfactory (less stable) antigens than the pervaporation-centrifugation technique.

[Poliovirus D antigen exists as both infectious and non-infectious particles. Hence there is not a constant relationship between D antigen and infectivity. In these studies only one precipitin line was observed and since native preparations were used it was probably a D rather than a C line. The abstracter can confirm the author's opinion that cadmium ions do not appear to enhance the precipitin lines in this system.]

A. J. Beale

GHENDON, I. Z. & MARCHENKO, A. T. **Comparative Investigation on the Pathogenicity for Monkeys and the Ability to Multiply at 40°C of Different Poliomyelitis Virus Strains.** *Acta Virologica.* Prague. 1961, Mar., v. 5, No. 2, 91–2.

It has been observed that strains of poliovirus which grow well at 40°C. are neurovirulent for monkeys and that those growing poorly at this temperature are avirulent. The authors investigated 111 strains and found in general that this correlation held good not only for standard virulent and attenuated vaccine strains but also for naturally occurring polioviruses. They did find, however, 8 strains (2 each of types 1 and 3, and 4 of type 2) which were non-pathogenic for monkeys despite their capacity to grow well at 40°C.

A. J. Beale

FROLOVA, M. P. & SAVINOV, A. P. **Histopathology of Experimental Infection of Rodents caused by the Karaganda AB Strain (Type IV Poliomyelitis Virus).** *Problems of Virology.* London. 1960, v. 5, No. 3, 337–44, 4 figs. [11 refs.] [Translated from Russian.]

The authors describe the histological lesions in rodents produced by the strain AB of a group of viruses isolated during a poliomyelitis epidemic in Karaganda, U.S.S.R. This virus was originally thought to represent a 4th serological type of poliovirus but subsequently proved to be serologically identical to Coxsackie A7 virus. The AB strain produced neuronal lesions in adult cotton rats similar to those produced by Lansing type 2 poliovirus. However, it produced much milder neuronal lesions in suckling mice and cotton rats and also lesions in voluntary muscles similar to those seen in Coxsackie A virus infections. The virus falls in spectrum of activity between neurotropic polioviruses and myotropic Coxsackie A viruses. The role of the AB strain in human disease is considered uncertain as yet.

[GRIST (this *Bulletin,* 1960, v. 35, 1059) has described the isolation of Coxsackie A7 virus from cases of "paralytic poliomyelitis" in Scotland under conditions strongly suggesting an aetiological relationship.]

A. J. Beale

SPRUNT, Katherine, KOENIG, Susan & ALEXANDER, Hattie E. **Factors influencing the Degree of Infectivity of Enterovirus Ribonucleic Acid (RNA). II. Role of Host Cell RNA Inactivators in the Low Degree of Infectivity of Poliovirus RNA in Low Salt Concentration.** *Virology.* New York. 1961, Jan., v. 13, No. 1, 135–8.

The authors have previously described how poliovirus RNA regains infectivity if hypertonic saline is substituted for isotonic [this *Bulletin,* 1960, v. 35, 713]. This reversal is not observed if the RNA has been in contact with human amnion cell monolayers. It was presumed that the RNA was destroyed by RNAase. Removal or reduction of this RNAase by repeated washing, either with saline or with heparin or yeast nucleic acid which block RNAase, did not restore the susceptibility of amnion cells to poliovirus RNA in isotonic solution to the level in hypertonic saline. It is concluded, therefore, that while such RNAase may play some role in preventing poliovirus RNA in isotonic solution from infecting cells this is not the major factor.

A. J. Beale

SLONIM, D., CINNEROVÁ, O., DREVO, M., MICHL, J. & MARES, I., with the technical assistance of K. DUBSKÁ, J. SPURNÁ & M. WACHTLOVÁ. **Some Experiences with the Preparation of Inactivated Poliomyelitis Vaccine in Czechoslovakia. III. Tissue Cultures.** *Acta Virologica.* Prague. 1961, Mar., v. 5, No. 2, 117–27, 3 figs. [11 refs.]

This is a long and detailed account of the factors effecting the success of trypsinization of monkey kidney cells. A procedure based on these investigations is described and usually yields 35 million cells per gm. of kidney tissue. One Roux bottle is seeded with 10 million such cells. During the process only 4 trypsinization cycles are carried out taking in all about 2 hours at 24 to 28°C. Trypsin was found to be superior to versene for the removal of monolayer cultures from Roux bottles before reseeding in tubes or other bottles.

[This is a very interesting paper which should be read in the original by anyone concerned with trypsinization—anyway if they are not satisfied with present results.] *A. J. Beale*

STUART, D. C., Jr. & FOGH, J. **Micromorphology of FL Cells infected with Polio and Coxsackie Viruses.** *Virology.* New York. 1961, Feb., v. 13, No. 2, 177–90, 17 figs. [10 refs.]

This paper consists essentially of 17 fascinating electronmicrographs showing stages in the development of Coxsackie B5 and poliomyelitis type 1 viruses in FL human amnion cells. The appearances were similar for both viruses. Virus appears to develop in close association with membranes in the cell which normally have ribonucleoprotein granules attached to them. The virus particles and normal ribonucleoprotein granules of the cell are similar in size and orientation to cellular membranes. The virus particles accumulate as crystal masses in the cytoplasm. Nuclear changes were seen in the nucleolus which became a large, loosely reticular body. The mitochondria became enlarged, swollen and distorted.

[The pictures should be examined as no short description can do them justice.] *A. J. Beale*

BERGE, T. O., BANKS, I. S. & TIGERTT, W. D. **Attenuation of Venezuelan Equine Encephalomyelitis Virus by *in vitro* Cultivation in Guinea-Pig Heart Cells.** *Amer. J. Hyg.* 1961, Mar., v. 73, No. 2, 209–18. [21 refs.]

The Trinidad strain of VEE virus was passaged in guineapig heart cells. With early passage material the ID50 and LD50 in mice by intracerebral or intraperitoneal inoculation were the same and similarly after 9 and 20 passages. After 26, 31 and 40 passages some mice surviving intracerebral infection were found to have been immunized. From the 45th passage the majority of the mice infected intracerebrally survived although there was no reduction in titre by tissue culture titration. 50th passage material multiplied in all the mouse tissues examined but virus was not detected in brain 7 days after infection. By intraperitoneal titration loss of virulence was detected by the 9th passage and markedly reduced by the 35th–40th passages. After 3 serial mouse brain passages of 50th tissue culture passage material the ability to kill mice by the intracerebral route was regained. After 9 mouse-brain passages however the virulence by the intraperitoneal route remained modified.

C. E. Gordon Smith

MCINTOSH, B. M., WORTH, C. B. & KOKERNOT, R. H. **Isolation of Semliki Forest Virus from *Aedes (Aedimorphus) argenteopunctatus* (Theobald) collected in Portuguese East Africa.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1961, Mar., v. 55, No. 2, 192–8. [19 refs.]

A pool of 97 *Aedes* (*Aedimorphus*) *argenteopunctatus* taken in April 1959 at Namacurra in Portuguese East Africa was inoculated into 2-day mice. 2–6 days later 5 mice died and from a sick mouse on the 6th day brain passages were made. After passage this virus (AR 2066) killed baby mice in 1 day and was found to be Seitz filterable. 3rd to 6th passage virus affected only 7 of 30 adult mice inoculated intracerebrally. A vervet monkey was given 30,000 LD50 intracerebrally—it had a temperature of 103·6°F. on the 2nd day when it circulated 3·5 log of virus. Similar inoculation of guineapigs caused no symptoms but high antibody titres. Haemagglutinins were obtained by sucrose-acetone extraction of brain or acetone-ether extraction of serum from sick suckling mice. Cross haemagglutinin-inhibition tests and cross complement-fixation tests showed a close relationship between AR 2066 and only Semliki Forest virus. By cross neutralization tests AR 2066 was shown to be related to other group A viruses: Mayaro and Chikungunya as well as Semliki.

Neutralizing antibody to Semliki virus had previously been found in human antibody surveys in northern Natal [this *Bulletin*, 1959, v. 34, 1089] and Portuguese East Africa: 20 of 306 and 44 of 837 sera from 2 collections. 17 sera with Semliki neutralizing antibody were tested against Mayaro and Chikungunya viruses—5 Chikungunya positives and 1 positive and 1 partial positive against Mayaro were found. 12 were positive only against Semliki virus. 30 sera from Namacurra collected at the same time as the mosquitoes were tested against the same viruses: 8 had neutralizing antibody against Semliki and/or Mayaro: in each case however the neutralizing index was highest against Chikungunya. Probably more than 1 group A virus is present in the area.

This is the first isolation of Semliki virus in Southern Africa and also the first isolation of a virus from *Aedes argenteopunctatus.* *C. E. Gordon Smith*

SHOPE, R. E. **An Immunizing Substance for Semliki Forest Virus in the Livers of Immune Mice. I. The Initial Observation together with a Consideration of the Attending Conditions.** *J. Exper. Med.* 1961, Mar. 1, v. 113, No. 3, 511–15.

Mice infected with *Trichinella spiralis* were infected subcutaneously with Semliki Forest virus then saved

by prompt treatment with helenine [this *Bulletin*, 1953, v. 28, 976]. 15 days after infection with virus their muscle, brains, livers and spleens were removed, ground up and inoculated intraperitoneally into 15 mice; 8 days later they received a second dose. 2 weeks later they were challenged with 100 MLD Semliki virus subcutaneously. All 8 control mice died but 7 of the 15 survived. This experiment was repeated by comparing trichinous and normal mice saved from Semliki infection, and their various tissues were inoculated separately. Only mice inoculated with liver from normal and trichinous mice were protected significantly from challenge. 14 days after challenge the livers and brains of the liver-inoculated mice and of 2 surviving control mice were used to inoculate mice in the same way. Both liver preparations protected mice against challenge. Subsequent experiments have shown that this immunizing effect is not due to traces of live virus [but details are not given]. The nature of the material causing the effect is not yet known. *C. E. Gordon Smith*

Beasley, Annie R., Lichter, W. & Sigel, M. M. **Studies on Latent Infections of Tissue Cultures with Dengue Virus. I. Characteristics of the System.** *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 5, 672–83. [17 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 906.]

Diercks, F. H., Kundin, W. D. & Porter, T. J. **Arthropod-Borne Virus Hemagglutinin Production by Infected Hamster Kidney-Cell Cultures.** *Amer. J. Hyg.* 1961, Mar., v. 73, No. 2, 164–72, 2 figs. [23 refs.]

The Nakayama strain of Japanese encephalitis virus after 70–80 mouse passages was used in trypsinized hamster kidney cultures. 5 serial passages were made and infectivity titres of 5·8–7·0 log and haemagglutinin (HA) titres of 16–32 obtained in all passages. The horse sera used in media were found to contain variable amounts of non-specific HA inhibitor. Sera from other species were also examined and heating was found to increase the inhibitor in guineapig, human and rabbit sera. In cultures infected with 10 TCD50, infectivity appeared after 24 hours and rose to a maximum of about 6 log after 96 hours while HA appeared after 96 hours (16–64). In cultures infected with 100,000 TCD50 maximum infectivity (about 7 log) was reached after about 40 hours and HA appeared at 32 hours (32–128). HA from the cultures was compared with suckling mouse brain HA extracted with acetone-ether at various *p*Hs and temperatures. Culture HA had a narrower *p*H range of activity at 4° and 25°C. but higher titres and a wide range at 37°C.

Russian spring-summer, Murray Valley, Ilheus, Uruma and yellow fever (17D) viruses were also shown to multiply in the cultures and produce HA. Less consistent results were obtained with Sicilian sandfly, Zika, Uganda S, Bwamba viruses, and no evidence of growth obtained with Naples sandfly and dengue viruses. *C. E. Gordon Smith*

Lee, H. W. & Scherer, W. F. **The Anamnestic Antibody Response to Japanese Encephalitis Virus in Monkeys and its Implications concerning Naturally Acquired Immunity in Man.** *J. Immunology.* 1961, Feb., v. 86, No. 2, 151–64, 5 figs. [22 refs.]

Cynomolgus monkeys without Japanese encephalitis (JE) antibody were inoculated intradermally with 8–9600 suckling mouse LD50 of mosquito suspension infected with JE. 1 of 2 monkeys tested on day 1 and all monkeys tested on days 2–5 had viraemia, maximum titre 2·2 log. Haemagglutinin-inhibiting antibody was usually detected by day 14. Complement-fixing and neutralizing antibody were also formed and all types of antibody persisted for up to at least 338 days. On a basis of viraemia and antibody response the ID50 for monkeys was 25–50 suckling mouse LD50. Virus was detected in the skin at the site of intradermal inoculation within 10 minutes but not in blood or lymph nodes. 12–16 hours after it was not detected in the skin or underlying muscle but in the blood and lymph node.

Previously infected monkeys were re-infected with various doses of JE mosquito suspensions and the antibody responses studied. Anamnestic responses in all types of antibody occurred and the ID50 was found to be 6–63 suckling mouse LD50. Anamnestic responses were also detected after 3rd and 4th infections with JE and no relationship was found between response and pre-existing antibody level. No viraemia was detected in re-infected monkeys and although virus could be detected in the skin at the site of inoculation within 10 minutes it was not found in blood or lymph nodes later.

Anamnestic antibody responses were also detected after inoculation of as little as 3·2 log LD50 of ultraviolet-inactivated virus. *C. E. Gordon Smith*

Nosek, J., Gresíková, M. & Řehácek, J. **Persistence of Tick-Borne Encephalitis Virus in Hibernating Bats.** *Acta Virologica.* Prague. 1961, Mar., v. 5, No. 2, 112–16, 2 figs. on pl. [12 refs.]

120 hibernating bats (*Myotis myotis, Barbastella barbastellus, Plecotus auritus*) were inoculated subcutaneously in the scapular region with 200,000 mouse LD50 of the 55/56th mouse passage of Hypr strain virus. They were maintained in hibernation in a cave at 8°C. and 100% relative humidity. After 23 days in 1 experiment and 30 in the other the bats were removed to room temperature. Bats were killed at intervals and blood, brain and liver examined for virus. Apart from a failure to react to stimuli and refusal to feed and drink in a few bats no symptoms were seen after hibernation. During hibernation virus was found in blood, brain and liver from the 2nd to the 12th day and in blood up to 23 days after inoculation. When the bats were moved to room temperature virus was found in the spleen and liver up to 11 days and in the brain up to 14 days later. Viraemia reached titres as high as 4·5 and 6·5 log and persisted for up to 7 days.

C. E. Gordon Smith

BÁRDOS, V.,* ČUPKOVÁ, E. & ŠEFCOVICOVÁ, L. **The Tahyna Virus. II. Characteristics of some Biological Properties and Preliminary Immunological Classification.** *Acta Virologica.* Prague. 1961, Mar., v. 5, No. 2, 93–100. [14 refs.]

Strain 92 [? passage level] titred 5·5 log intracerebrally (IC) and < 1 log intraperitoneally (IP) in young adult mice. It titred 7 log IC and 4·7 log subcutaneously (SC) in sucklings. Strains 163 and 263 titred 7·3 and 7·6 log IC in sucklings. Extraneural strain 236 [this *Bulletin*, 1961, v. 36, 506] killed young adults in 5–8 days at a dose of 4·5 log suckling LD50 IC up to 11 passages but 236 maintained by mouse brain passage at a dose of 3·6 log LD50 killed young adults in 4 days after 7 passages. Suckling rats died 3–5 days after IC inoculation of strain 92, 5–7 days after SC inoculation. Adult hamsters died 8–9 days after IC inoculation. Adult rats, guineapigs and rabbits showed no symptoms but formed antibody. A horse given 5·9 LD50 of strain 92 [? SC] showed no symptoms but had antibody from 7 days after infection. 2 pigs given extraneural 236 SC showed no symptoms but had antibody from 4 days after infection.

3 of 4 chick embryos inoculated by the yolk sac with strain 92 died 5–8 days later—in the next passage all embryos died after 5–9 days. 5·8 log LD50 of extraneural 236 killed embryos in 5–6 days. The titres of the embryos in young adult mice were 4·3 –4·5 log.

2·5 and 3·5 log LD50 of strain 92 caused cytopathic effects in hamster kidney culture after 48–72 hours and the TCD50 was not more than 1 log lower than the ICLD50 in young adult mice of mouse brain suspensions. Titres of 3·5–4·5 log TCD50 were found in the culture medium. Similar results were obtained in chick embryo cultures. In human amnion cells cytopathic effects were irregular but the virus could be passaged and titres of 3 log LD50 were found in the medium. Similar titres without cytopathic effect were found in cynomolgus monkey heart and KB cell cultures.

Histological examination of infected mouse tissues revealed encephalitis but no lesions in spinal cord or other organs.

Haemagglutinins and complement-fixing antigens were prepared by acetone-ether or saccharose-acetone extractions of infected suckling mouse brain. These reacted with homologous antisera but no cross reaction was found with a number of viruses in groups A and B. In neutralization tests against hyperimmune sera to 22 arthropod-borne viruses no relationship was demonstrated.

C. E. Gordon Smith

KOKERNOT, R. H., SMITHBURN, K. C. & KLUGE, E. **Neutralizing Antibodies against Arthropod-Borne Viruses in the Sera of Domestic Quadrupeds ranging in Tongaland, Union of South Africa.** *Ann. Trop. Med. & Parasit.* 1961, Apr., v. 55, No. 1, 73–85, 1 fig. [26 refs.]

Sera were collected from cattle and goats at 11 places and sheep at 8 places scattered throughout Tongaland. The ages of the animals were estimated from their teeth. They were tested for neutralizing antibody to Chikungunya and Sindbis viruses intracerebrally (IC) and to Middelburg intraperitoneally (IP) in suckling mice; to Semliki Forest, West Nile, Bunyamwera and Pongola IC in adult mice and to Rift Valley virus IP in infant and adult mice. Mice of both ages were used in IC tests with Wesselsbron, H 336, and Spondweni viruses. Protection against at least 50 LD50 was accepted as positive.

The highest numbers of positive sera in mountain, river pan and coastal areas were found against Middelburg (12, 18, 24%) Wesselsbron (14, 50 42%) and Bunyamwera (9, 13, 13%). Very few sera from the mountain zone had antibody against the other viruses. For the river pan area, 10% and 20% had Rift Valley and Pongola antibody respectively and about 2% had antibody for each of the others except Chikungunya. On the coastal plain 16% and 6% had Rift Valley and Pongola antibody, 13% and 10% West Nile and H 336 antibody respectively. 1–3% had antibody to the others except Chikungunya. Monotypic protection was found in all species against Semliki and in cattle only against Sindbis. 25% of goats, 18% of sheep and 11% of cattle had Middelburg antibody. Most positive sera against group B viruses were positive only against Wesselsbron. No goat sera protected against West Nile or H 336. Monotypic protection against Spondweni, and H 336 were found in sheep and against Spondweni H 336, West Nile and Wesselsbron in cattle. Bunyamwera antibody was widespread and similar in incidence in the 3 species. 10% of cattle, 11% of goats and 3% of sheep had Rift Valley antibody. With Pongola virus 6%, 10% and 9% were positive respectively. Sera from dogs and donkeys were tested from Lake Simbu. Donkeys had antibody to Middelburg (12/28), Semliki (7/30), Chikungunya (4/30), Spondweni (1/30), Wesselsbron (27/30), H 336 (4/30), Bunyamwera (16/21), Pongola (21/30) and Bwamba (8/30) viruses. Dogs had antibody to Middelburg (1/7) and Wesselsbron (5/7) only.

[See also this *Bulletin*, 1959, v. 34, 1089.]

C. E. Gordon Smith

MEDVEDEVA, G. I. **Comparative Study of the Immunological Aspects of Live Yellow Fever Vaccines.** *Problems of Virology.* London. 1960, v. 5, No. 4, 476–81, 3 figs. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 905.]

GILLESPIE, J. H. & KARZON, D. T. **A Study of the Relationship between Canine Distemper and Measles in the Dog.** *Proc. Soc. Exper. Biol. & Med.* 1960, Dec., v. 105, No. 3, 547–51. [13 refs.]

The authors have investigated the antigenic relationship between measles and canine distemper in young

dogs 5–24 weeks of age, inoculated with live measles virus and subsequently challenged with virulent distemper virus. 6 dogs injected intravenously with about 10^5 TCD50 of the Edmonston strain of measles virus showed no clinical response to infection over a period of 24–28 days; they developed measles neutralizing antibody in titres of 64 to over 256, but distemper neutralizing antibody appeared in 2 dogs only, in titres of 5 and 7 respectively. After intravenous challenge with the Snyder Hill strain of distemper virus no signs of illness were observed; distemper neutralizing antibody appeared in titres of 400–300,000, whereas the titres of measles neutralizing antibody remained relatively unaffected. 3 control animals all developed a febrile illness after infection with distemper virus, and 1 died.

Similar results were obtained with 3 dogs and their corresponding controls challenged with distemper virus 84 days after infection with measles virus. 3 other dogs infected with measles virus developed measles antibody, and distemper antibody in titres of 28 and 30; on intracerebral challenge with distemper virus after 45 days 2 developed a febrile illness, and distemper antibody appeared in all 3 titres of 60, 300,000 and 3,000,000.

The results thus show that infection with measles virus will produce low titres of distemper neutralizing antibody and will protect dogs against subsequent challenge with distemper virus, and provide further evidence of an antigenic relationship between the two viruses. *D. J. Bauer*

DeMeio, J. L. & Gower, T. A. **Hemagglutination by Measles Virus.** *Virology.* New York. 1961, Mar., v. 13, No. 3, 367–8.

Yoshino, K.; Kondo, Akira; Kuma, N.; Taniguchi, H.; Suzuki, M. **Infection of the One-Day Old Fertile Hen's Egg with Rabies Virus. VI. Strain Differences in the Egg Adaptability** [Yoshino, Kondo, Kuma & Taniguchi]. *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 5, 684–97, 5 figs. [11 refs.] **VII. Comparison of Viral Yields obtained by Inoculation of Eggs of Different Ages with Different Strains and Production of Vaccine** [Yoshino, Suzuki & Kondo]. *Ibid.*, 698–711, 6 figs. [21 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 906.]

Bellett, A. J. D. & Burness, A. T. H. **Nature of the 'Infective Ribonucleic Acid Component' in Cells infected with Encephalomyocarditis Virus and the 'Virosome' Concept.** *Nature.* 1961, Apr. 15, v. 190, 235–7.

Ribonucleic acid extracted from ascites tumour cells infected with mouse encephalomyocarditis virus was used to infect further cells which were then exposed to the action of ribonuclease in a concentration of 1 μgm. per ml. The number of cells which produced virus was reduced to 100-fold by this treatment in comparison with control cells infected with ribonucleic acid but not treated with the enzyme. The latter, however, had no effect upon the yield in cells infected with virus, a result which suggests that the ribonucleic acid which can be extracted with phenol from cells infected with encephalomyocarditis virus is not accessible to the action of ribonuclease. The enzyme also failed to reduce the infectivity of ribonucleic acid isolated from various cell components in cells which had been disrupted by osmotic shock. Treatment with papain of material from infected cells obtained by high-speed centrifugation rendered the ribonucleic acid contained in it somewhat more sensitive to the action of ribonuclease; it was therefore concluded that the ribonucleic acid of the infected cell is protected by combination with protein, and it is postulated that this combination occurs in the form of particles of ribonucleoprotein, for which the name "virosome" is proposed. *D. J. Bauer*

IMMUNITY

Guthrie, R. K., Dowdy, J. R. & Hinkle, D. C. **Effects of Lipid Materials on Guinea Pig Complement.** *Canadian J. Biochem. & Physiol.* 1961, Apr., v. 39, No. 4, 757–62. [13 refs.]

"Prior work has shown that the fourth component of guinea pig complement is increased following antigen injection. This report concerns the changes in C'4 following injection of non-antigenic materials. Injection of cholesterol, ergosterol, or linoleic acid does not cause any measurable change in C' or C'4. Injection of oleic or of stearic acid causes a significant increase in C'4 but has no effect on C'."

Haas, R. & Thomssen, R. Über den Entwicklungsstand der in der Immunbiologie gebräuchlichen Adjuvantien. [**The Development of Adjuvants Commonly Used in Immunobiology**] *Ergebn. Mikrobiol. Immunitätsf.* 1961, v. 34, 27–119, 18 figs. [Numerous refs.]

A review of the subject.

Haurowitz, F. **Use of Radioisotopes in Immunochemical Research.** *Ergebn. Mikrobiol. Immunitätsf.* 1961, v. 34, 1–26, 5 figs. [Numerous refs.]

A review of the subject.

WARD, P. A., ABELL, M. R. & JOHNSON, A. G. **Studies on the Adjuvant Action of Bacterial Endotoxins on Antibody Formation. IV. Histologic Study of Cortisone-Treated Rabbits.** *Amer. J. Path.* 1961, Feb., v. 38, No. 2, 189–205, 12 figs. on 4 pls. [16 refs.]

In a previous paper [this *Bulletin*, 1959, v. 34, (841)] the authors described the histological changes in spleens of rabbits following a single injection of bovine gamma globulin alone and in combination with an adjuvant (bacterial endotoxin). They had also established [*ibid.*, 1199] that the potent adjuvant action of endotoxins derived from Gram-negative bacteria could stimulate the synthesis of antibody to human serum albumin in rabbits given inhibitory doses of cortisone. The present investigation was carried out to ascertain the location and cell type of the lesions in spleens of rabbits treated with cortisone and given injection of antigen with and without stimulation by endotoxins.

The primary antibody response incited by the adjuvant action of endotoxin in cortisone-treated rabbits was associated with the appearance and proliferation of modified (pyroninophilic) reticular cells in the centres of splenic follicles: this substantiates the hypothesis that changes in the germinal centres of follicles in the lymph nodes and spleen are associated with the production of antibody. The number of mitotic figures and the degree of pyroninophilia within splenic follicles were correlated with the level of serum antibody. On the other hand, only trace amounts of haemugglutinating antibody were observed in cortisone-treated animals receiving antigen but not endotoxin. Circulating antibody and the follicular response, consisting of proliferation and differentiation of primitive reticular cells, were prominent only when endotoxin was given in combination with antigen. The fact that little or no antibody appeared in the cortisone-treated rabbits receiving only the antigen, despite the apparent morphological normality of these cells, implies that cortisone inhibition of antibody production takes place by means other than by detectable structural cellular damage. An additional property of cortisone, that of inhibition of mitosis, may also play a role in suppressing the antibody response.

The authors believe that the fact that antibody production (under endotoxin stimulation) proceeded in the virtual absence of mature lymphocytes tends to negate the importance of this cell *per se*, as being significant in the production of antibody under their experimental conditions, and any role played by plasma cells or the red pulp of the spleen was not apparent.

D. A. Cannon

ASHERSON, G. L. & BROBERGER, O. **Incidence of Haemagglutinating and Complement-Fixing Antibodies.** *Brit. Med. J.* 1961, May 20, 1429–33. [20 refs.]

HINZ, C. F., JR., WEDGWOOD, R. J. & PILLEMER, L. **The Properdin System and Immunity. XV. Some Biologic Effects of the Administration of Zymosan and other Polysaccharides to Rabbits, and the Presence of Antibodies to Zymosan in Human and Rabbit Serum.** *J. Lab. & Clin. Med.* 1961, Feb., v. 57, No. 2, 185–98, 5 figs. [27 refs.]

"1. The injection into rabbits of zymosan and other high molecular weight polysaccharides caused a fall in properdin level and C'3 level in serum.

"2. The ability to produce these effects in vivo correlated with the ability of these agents to combine with properdin in vitro.

"3. The injection of zymosan and dextran produced fever and leukopenia similar to that caused by endotoxin, but the properdin level of the recipient animal did not affect pyrogenic or leukopenic responses.

"4. Zymosan and those dextrans which interact with properdin were effective in provoking the local Shwartzman reaction, but did not serve as the preparatory agent for the local Shwartzman reaction.

"5. The properties for combination with properdin are probably not directly related to endotoxic properties inherent in or contaminating the polysaccharide preparations.

"6. Injection of zymosan into rabbits caused the appearance of an antibody to zymosan. Some human sera spontaneously contained agglutinins for zymosan.

"7. The antibody to zymosan could be clearly distinguished from properdin itself."

GENGOZIAN, N., MAKINODAN, T. & SHEKARCHI, I. C. **Transplantation of Antibody-Forming Cells in Lethally Irradiated Mice.** *J. Immunology.* 1961, Feb., v. 86, No. 2, 113–22, 4 figs. [43 refs.]

"A comprehensive study of the relative contribution of normal versus presensitized bone marrow or spleen tissue to the antibody-forming mechanisms of lethally irradiated mice was made. Bone marrow cells transplanted into the irradiated animals showed definite antibody-forming potential when marrow was obtained from presensitized donors but lacked this capacity if normal, nonsensitized donors were used. In contrast, both normal and presensitized spleen cells transplanted into the irradiated host were able to initiate an immune response to the test antigen. The marked efficiency of the spleen over the bone marrow was indicated by the ability of 12×10^6 presensitized spleen cells to produce agglutinins in amounts comparable to that observed in normal mice undergoing a secondary type of response. Different presensitization procedures of the donors also revealed differences in the efficiency of the transplanted hematopoietic cells to produce antibody in the irradiated host.

"The increased antibody-forming potential of both bone marrow and spleen cells from presensitized donors was demonstrated in two *in vivo* biologic tests: (a) there was a relative decrease in the ability of marrow and spleen cells from presensitized donors to protect lethally irradiated isologous mice; and (b) in a homologous transfer of cells, marrow and spleen cells from

donors sensitized to the homologous recipient showed a detrimental effect when transplanted into lethally irradiated homologous mice."

COLLI, A., OPFERKUCH, W. & KLEIN, P. Studien über den Mechanismus der Immunhämolyse: Der Bindungsmodus der vierten Komplementkomponente. **[Studies on the Mechanism of Immune Haemolysis; the Nature of the Combination of the Fourth Component of Complement]** *Ztschr. f. Hyg. u. Infektionskr.* 1961, v. 147, No. 3, 213–29, 3 figs. [11 refs.]

If complement is treated with hydrazine hydrate to remove the C'4 component it can subsequently be split into end and middle piece as in the usual fractionation of complement. The C'4 deficient residue of M piece can then be combined with sensitized sheep's red blood corpuscles (EA), so as to give the complex EAC'1, and EAC'1 readily takes up C'4 to give EAC'1–4 which can readily be lysed by R4, *i.e.* complement deficient in C'4 prepared as described above. This, therefore, is a two-phase reaction. The second, between EAC'1 and C'4, a very rapid one independent of temperature and of Ca ions, whereas the first, between EA and C'1, is a Ca-dependent reaction.

The product R4 obtained from complement by hydrazine hydrate treatment contains a factor which is destructive of a quality of C1 which is involved in the lysis of EAC'1–4 by R1. *J. W. McLeod*

OPFERKUCH, W., COLLI, A. & KLEIN, P. Studien über den Mechanismus der Immunhämolyse: Die Bindung der zweiten Komplementkomponente. **[Studies on the Mechanism of Immune Haemolysis: Combination of the Second Component of Complement]** *Ztschr. f. Hyg. u. Infektionskr.* 1961, v. 147, No. 3, 230–39, 3 figs. [10 refs.]

The authors operate with (i)—sensitized sheep's blood (AE) treated successively with ether-inactivated and heat-inactivated complement, as a source of $EAC'_{1,}$ and devoid of C'2 and C'3: (ii)—with eR_4, end piece separated from R_4 (*i.e.* complement stripped of component 4 by hydrazine hydrate) as source of component 2 only; and (iii)—R_4 absorbed with antibody-treated stromata so as to produce a reagent with active C'1 and C'3 components but devoid of C'1 and C'4.

Studying the combinations obtained with these th authors reach the conclusion that the reaction $EAC'_{1,}$ + C'2 is much increased at body temperature and i determined by combination of C'2 not only with C'1 but also with C'1. A diagram representing the typ of combination visualized is incorporated.

J. W. McLeod

NORTHOVER, B. J. **Influence of the Charge on a Serum Protein Molecule and its Ability to stimulate or inhibit the Phagocytosis of Bacteria by Leucocytes.** [Correspondence.] *Nature.* 1961 Feb. 18, v. 189, 574–6, 2 figs.

Using a modification of the slide-cell technique o WRIGHT to assess the phagocytic ability of human leucocytes towards bacteria, the author investigated the effect of various human serum proteins upon the phagocytosis of staphylococci by human leucocytes particularly with a view to showing the effect o modifying the net charge on the serum protein molecule upon the ability of the protein to stimulate or inhibit phagocytosis. His results show that, for a given protein, the more negative its charge the more inhibitory it is towards phagocytosis, and conversely, the less negative the charge the more it will stimulate phagocytosis. In the case of the globulins there seemed to be the potentiality for either stimulation or inhibition of phagocytosis; but the albumins seemed to be capable only of inhibition. He decided therefore that there are other properties of a protein molecule besides its charge which determine its effect upon phagocytosis.

D. A. Cannon

Miscellaneous

METROPOLITAN HOSPITAL PLANNING COUNCIL. **Hospital Utilization in the Metropolitan Area of the Lower Mainland. A Study of the Referral Patterns in Operation in the Province of British Columbia, 1960.** Numerous mimeographed pp., illustrated. 1961. Vancouver 8: 301, Wesbrook Building, University of British Columbia, B.C., Canada.

This report discusses the pattern of hospital utilization in the Lower Mainland of British Columbia. It is a statistical study of hospital transfers, hospital referrals, place of residence, place of hospitalization, as well as an account of some factors involved in hospitalization.

The study was undertaken in order to provide facts for the consideration of the detailed planning of an integrated hospital service in the region. The authors have only studied, as indeed they set out to do, the patterns of referral and have not attempted to discover any hidden or suppressed needs for hospital care.

M. D. Warren

Book Reviews

PALLASKE, G. **Pathologische Anatomie und Pathogenese der spontanen Tuberkulose der Tiere.** [The Pathological Anatomy and Pathogenesis of Spontaneous Tuberculosis in Animals.] pp. x + 152, 48 figs. (12 coloured) on 8 pls. 1961. Stuttgart: Gustav Fischer Verlag, Stafflenbergstrasse 36. [DM28.–.]

In about 150 pages of small type accounts are found of the pathogenesis of spontaneous tuberculosis in the domesticated animals such as cattle, sheep, goats, horses, pigs, dogs and cats. Other sections are given up to the disease in small laboratory animals such as rabbits, guineapigs and mice, while others tell us about the condition in wild carnivores bred for their pelts, in monkeys and other animals kept in zoological gardens and in domesticated and other birds.

Special attention is paid to the portals of entry of the organism and their relationship to the subsequent development and importance of the primary complexes. The nature of the changes which follow in the infected animal and the spread within the body are described. The species of animal, that is the host, plays the greater part in determining the nature and appearance of the lesions; although the avian type of bacillus may influence these considerations, especially in the pig, the question as to whether the infective bacillus is of the human or bovine type is of secondary importance. Consequently the author gives separate accounts of the disease in cattle according to whether the host is a calf, a young animal or an adult.

The type of lesion is also influenced by the organ in which it occurs and this, as well as any hypersensitivity enjoyed by the animal, is discussed.

All of these questions are dealt with under general headings before consideration is given to them under the species-of-animal sections. The book is a scholarly monograph and the title is an apt description of its contents. It contains 5½ pages of references, largely of continental origin, and 48 figures. The figures are mostly of the macroscopic appearances of tuberculous lesions and 12 of them are in colour. The transference of infection between man and animals is not lost sight of and consideration is given to the pathological anatomy of tuberculosis in animals slaughtered for food and of the other dangers which occur in man's association with animals when either may be tuberculous. *R. Lovell*

AMERICAN PUBLIC HEALTH ASSOCIATION. **Standard Methods for the Examination of Water and Waste-Water including Bottom Sediments and Sludges. Prepared and published jointly by American Public Health Association and American Water Works Association, and Water Pollution Control Federation. 11th Edition.** pp. xxi + 626, 58 figs. & 20 pls. 1960. New York 19: Amer. Pub. Health Ass., Inc., 1790 Broadway. [77s.]

"The first edition of *Standard Methods* was published in 1905." At intervals since then revised and enlarged editions have appeared [see this *Bulletin*, 1955, v. 30, 732] till this the 11th edition has been reached. Its publication is under the auspices of a Joint Editorial Board of the American Public Health Association, the American Water Works Association and the Water Pollution Control Federation with assistance from other associations and experts.

It is noted that in order to describe more accurately and concisely the contents of the eleventh edition, the title has been changed to "Standard Methods for the Examination of Water and Wastewater".

The important preface refers to the numerous revisions and additions that have been made in the different parts of the book which include an infra-red method for the determination of synthetic detergents. There are also 3 new parts in this edition—procedures for the measurement of radioactivity in water and wastes (Part V); improved techniques for the detection and isolation of iron and sulphur bacteria (Part VIII) and bioassay methods for the evalution of acute toxicity of industrial wastes and other substances to fish (Part VI).

This edition contains a General Introduction comprising much important information on apparatus, reagents and techniques; expression of analytical results; precision and accuracy; and includes a section on the statistical approach and graphical representation of data.

Each method of examination is clearly and accurately described whether it be of chemical, physical, bacteriological or other biological nature with an appended bibliography. Diagrams, figures, tables and illustrations are used freely.

It is to be noted that all the methods described are "Standard" unless designated as "Tentative". The former have been "extensively studied and accepted as applicable within the limits of sensitivity, precision and accuracy recorded", whereas "Tentative" methods are those still under investigation which have not yet been fully evaluated.

This manual is admirably produced and will be a most valuable publication. *M. E. Delafield*

MACQUEEN, Ian A. G. [M.A., M.D., D.P.H., F.R.S.H.] **A Study of Home Accidents in Aberdeen. An Investigation financed by the Nuffield Provincial Hospitals Trust.** pp. viii + 100, 10 figs. 1960. Edinburgh. London: E. & S. Livingstone Ltd.

This excellent book contains an account of the results of a study of home accidents in Aberdeen of which there occurred 4,527 between September 1, 1955 and August 31, 1957. The study was made possible by a generous grant from the Nuffield Provincial Hospitals Trust.

Throughout these 2 years, the Aberdeen hospitals, 46 general practitioners, and over 60 health visitors

informed the Health and Welfare Department of domestic accidents which came to their notice. A detailed investigation of these accidents was then carried out, records were made as uniformly as possible and the findings then analysed statistically.

There is a good introduction which describes the Home Safety Week organized by the Health and Welfare Department in 1954 followed by continuing home education by social workers. It also gives some particulars of the City which in mid-1957 had an estimated population of 186,190, a high density of 16·4 persons per acre, a high proportion of unskilled workers, a good deal of overcrowding and other housing problems.

A chapter contains a thoughtful discussion of the validity and reliability of the survey. There follow chapters which contain the findings of the survey given in detail with many tables and figures on (1) ages and sex differences, (2) types of accident, (3) variations of month, day and hour, (4) notification and treatment, (5) household conditions, (6) social features of accidents to children, (7) family and physical factors, (8) accident proneness and (9) potential causes of other accidents.

In the conclusions which are well-stated in a relatively short chapter, it is also mentioned that although the present survey was not primarily intended to measure the success of the Home Safety Campaign of Aberdeen nevertheless it provided a variety of evidence to the effect that this campaign has had very high success.

Appended are the recording forms used in the study and 20 tables of detailed statistical information. There is also a good index to this valuable book.

M. E. Delafield

NOTICE

HEALTH AND TUBERCULOSIS CONFERENCE

IBADAN, NIGERIA—MARCH 1962

The Chest and Heart Association, with the co-operation of the Federal Government of Nigeria is sponsoring a Health and Tuberculosis Conference to be held at the UNIVERSITY COLLEGE, IBADAN, NIGERIA from 26th–31st March, 1962.

The programme will include lectures and panel discussions on: Tuberculosis the greatest tropical menace, Tuberculosis and Leprosy, Community infection—cause and remedy, Drugs—their value and limitations, The techniques of community surveys, Non-pulmonary tuberculosis, Travelling clinics and village hygiene.

Applications for further details should be made to the Conference Secretary, The Chest and Heart Association, Tavistock House North, Tavistock Square, London, W.C.1.

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